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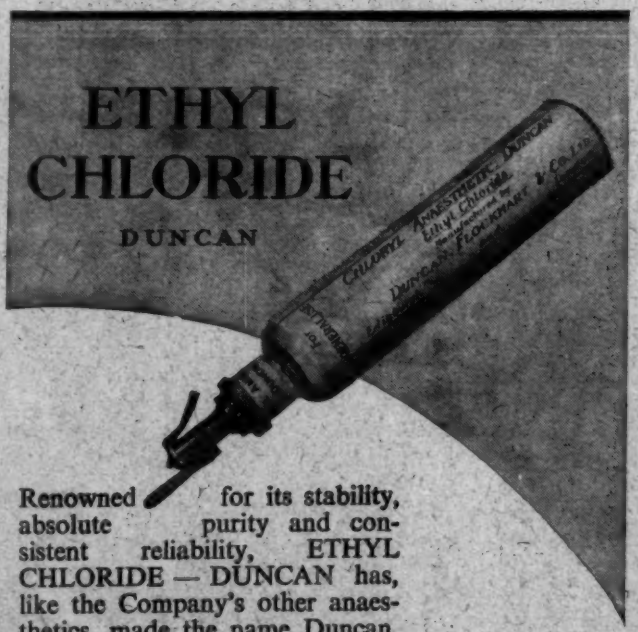

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 20 1952

STATISTICAL ASPECTS OF MORTALITY IN EARLY ADULT LIFE*

BY

R. C. GEARY

Director, Central Statistics Office, Dublin

For the purpose of the present paper early adult life has been taken as the age period 15–44 years. If this period seems unduly prolonged I may point out that it is used extensively in statistical literature, if not explicitly defined as "early adult life." The notion of the upper age limit of youth may tend to be positively correlated with the age of the lecturer, mindful of which I have tried to avoid prejudging the issue by analysing the data in subperiods, usually 15–24, 25–34, and 35–44.

To set the matter in statistical perspective, in Ireland† in 1949 the total number of deaths under 1 year of age was 3,400, or 9% of the total of 38,100 deaths at all ages; 1,200 (or 3% of total deaths) were in childhood (ages 1–14); 3,700 (or 10%) in early adult life as defined —namely, in the age group 15–44; 7,200 (or 19%) at the later adult ages 45–64; and the remaining 22,600 (or 59%) at ages 65 and over. To state, however, that "only" one-tenth of the total deaths occur at the early adult ages would be seriously to misconceive the qualitative character of the problem. We must all die some time, and there must be some lower limit to infantile mortality—perhaps some countries are near the absolute lower limit. But the elimination of all but a few deaths at young adult ages is surely a reasonable objective of preventive and curative medicine. As will presently be seen, the trend in recent years lends encouragement to such a hope.

Expectation of Life

It is a curious, even a paradoxical, fact that for want of the proper statistics we are prone to judge the condition of the public health by death rates alone. Even morbidity statistics are in an early stage of development, and we know practically nothing about the physical or mental health of the great majority of the public. In any group of the population in a period there are three divisions: (*a*) those who die, (*b*) those sick, and others unable to pursue a normal life (measured in suitable statistical units), and (*c*) the rest. The rest, especially at the age group 15–44 years, are the great majority. The fact that discussion on the state of the public health is practically confined, in its statistical aspect, to death rates, tends to produce a somewhat distorted picture in the public mind.

It is therefore essential to try to present the problem in its social perspective. At age 15 in Ireland in 1945–7 the expectation of life of males was 52.2 years. This represents the number of years, on the average, which men would expect to live after the age of 15. Perhaps it would be simpler to say that for those who have lived to age 15 the average age at death would be 67.2 years. The life table also shows that in the thirty-years span from ages 15 to 45 the average number of years lived by males would be 28.6 years. The figure would be 30 years if mortality were *nil*. Mortality in the age group 15–44 accordingly reduces the maximum span by only 1.4 years.‡ The corresponding figure for women is 1.5 years. There is no significant difference between urban and rural areas in this matter, since, for urban areas alone, years lost in the period of life under consideration are 1.5 for both men and women.

International Comparisons

Much of what I have to say is derived from Table I, which shows the death rates per 100,000 in 1899–1902 and 1947–9 in 16 countries for males, females, and total persons from all causes and from tuberculosis, and certain statistics derived therefrom. The main features of the table are illustrated in Diagram I. The rates shown in the table for each sex are generally the simple averages of the rates in the six quinquennial age groups 15–19 to 40–44 inclusive, which means that they are standardized to a population with the same numbers in each of the six age groups.

Column 7 shows that there is a marked variability between the countries in the young adult mortality rate, ranging from 449 for Spain to 163 for the Netherlands. Ireland is fourth highest on the list, and Scotland fifth. The range of variation is far greater for tuberculosis (column 10): from 185 for Portugal to 18 for Denmark, so that the Portuguese rate is no less than ten times the Danish rate. The rate of 128 for Ireland, exceeded by the rates for only three of the countries shown, is more than twice that for England and Wales and is seven times the Danish rate. Excluding tuberculosis (column 13), the range of variation, while less than that of the death rate from all causes (column 7), is still substantial. The exclusion of tuberculosis has the effect of bringing the Irish rate nearly level with the Scottish rate, and almost eliminates the difference between England and Wales, the Scandinavian countries, and the Netherlands.

Perhaps the outstanding feature of the table is shown by column 16. In all countries the decline in the death rate during the past half-century has been substantial,

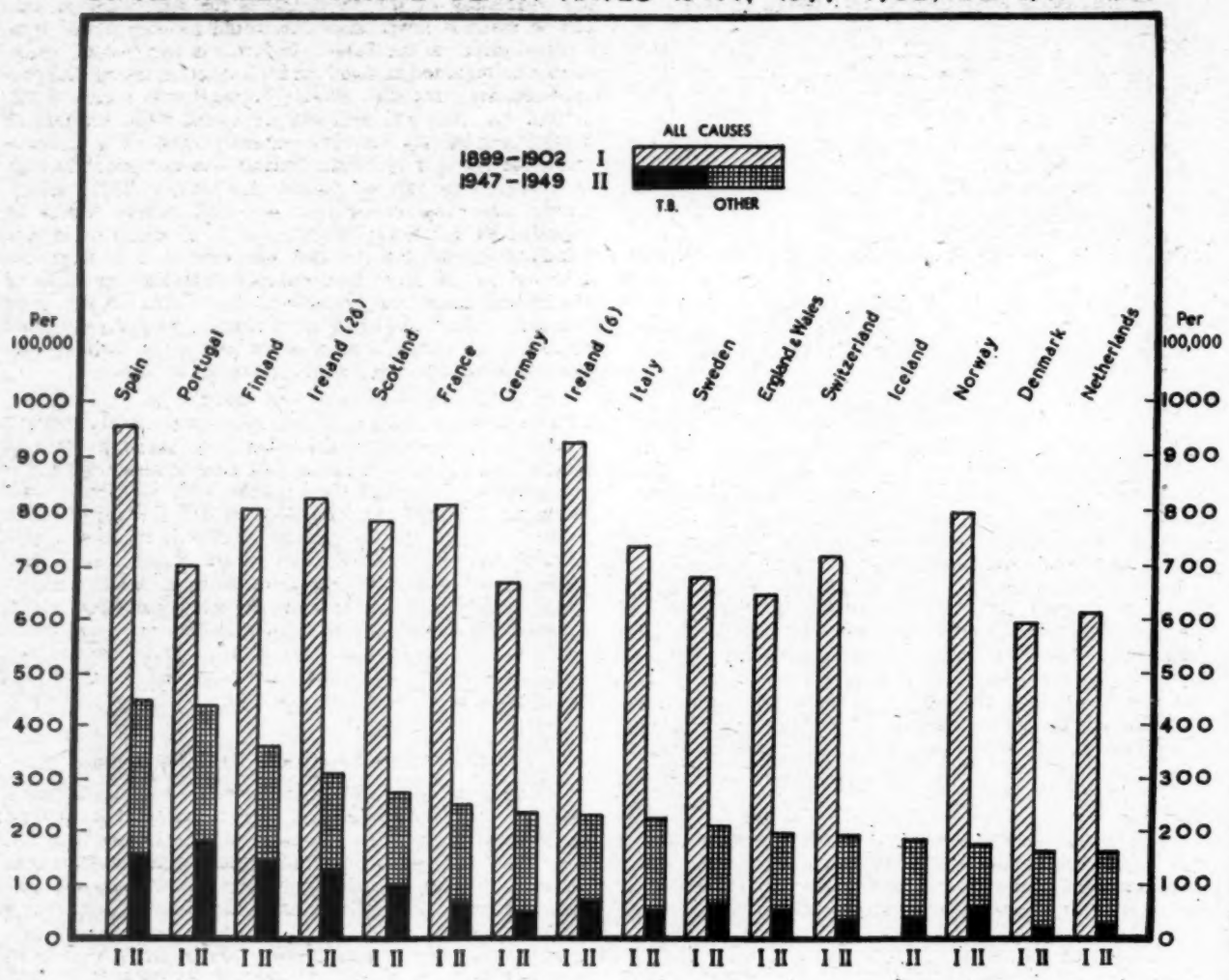
*Paper read at the Joint Annual Meeting of the British Medical Association and the Irish Medical Association, Dublin, 1952.

†Throughout the paper "Ireland" connotes the 26 counties.

‡It is now probably less than one.

DIAGRAM I.

STANDARDIZED ANNUAL DEATH RATES 15-44, 1899-1902, AND 1947-1949



ranging from 40% for Portugal to 78% for Norway, which means that in Norway the rate is now little more than one-fifth of what it was at the beginning of the century. Actually the general decline was well under way during the last part of the nineteenth century, for, as will be seen from Table III, in England and Wales the rate declined from 982 to 612 between the decades 1871–80 to 1901–10, and is now but one-third of its level at the start of the present century.

The trends for England and Wales and Ireland since the decade 1871–80 are shown in Diagram II (derived from Table III). The closeness to linearity of the downward gradient, over the whole period for England and Wales and since 1901–10 for Ireland, is remarkable. The reason for the change in gradient in Ireland at 1901–10 is not clearly evident : registration may have been incomplete in the decade 1871–80, which was not long after the year when registration started in Ireland—namely, 1864. If present trends continue there will be practically no young adult deaths in England and Wales by 1975 or in Ireland by 1980.

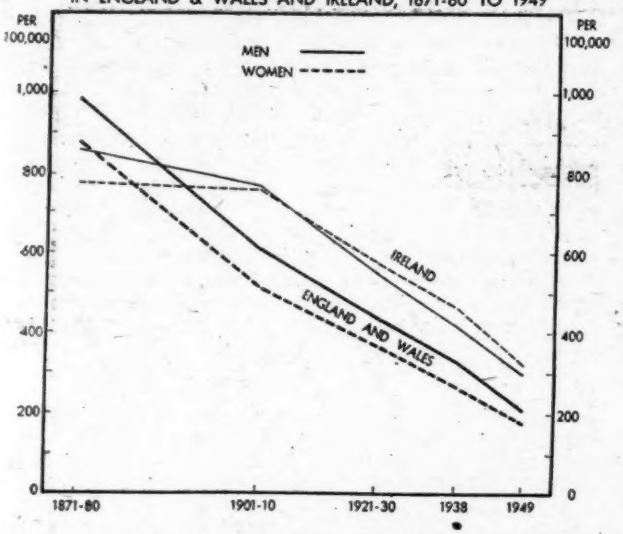
Column 17 shows that Ireland and Scotland are the only countries in which the female death rate exceeds the male. In Ireland the unfavourable expectation of life for females as compared with males has been commented upon in Census reports, though a significant improvement in this respect was recorded by the 1945–7 Life Table. As regards young adults, Ireland's higher death rates for women are a comparatively recent development, for up to 1910 or so Ireland conformed to the general pattern. We do not know the reason. It may be associated with the low marriage rate, though the Irish marriage rate has been low for nearly a century. Or it may be that emigration is selective, at any rate as regards healthy women. Ireland has not only an abnormally high emigration rate but it is also exceptional in the proportion of women in the emigration stream. Portugal, Finland, and Ireland have the highest figures for tuberculosis as percentage of total deaths at young adult ages (column 20). In these countries tuberculosis accounts for nearly half the total deaths at these ages. Comparison of columns 18 and 19 shows that in most countries the percentage is higher for women than for men.

General Inferences

This completes the purely descriptive features of Table I. To draw general inferences it will be necessary to use statistical techniques. A glance at the Table will show that the Scandinavian countries, England and Wales, and the Netherlands, with relatively high standards of living, have generally the lowest mortality rates in general and tuberculosis mortality rates in particular. In these countries also the *percentage* decline in the death rates is greater than the general

DIAGRAM II

STANDARDIZED ANNUAL DEATH RATES 15-44 IN ENGLAND & WALES AND IRELAND, 1871-80 TO 1949



average. Furthermore, in these countries the percentage borne by tuberculosis mortality in the general death rate is lower than the average. It is a remarkable and perhaps rather unexpected fact that the tuberculosis death rate in the years 1947–9 is highly correlated with the death rate from other causes. In fact $r=+0.81$. The odds against so high a value occurring in chance association of 16 pairs of numbers is less than 1/1,000. Does tuberculosis render the whole population less viable, apart from those who die from this disease? If so, will a successful campaign against tuberculosis have beneficial effects on health extending far beyond its specific limits and objectives? Or is the correlation due to a common factor affecting the tuberculosis rate as well as the other cause rate? If so, the most obvious common factor is the standard of living; even when this is eliminated the correlation remains high, at +0.63, which, with 9 d.f., may be regarded as significant ($0.02<P<0.05$).

As regards the relationship between the rate of decline and the level of mortality at the beginning of the century the correlation of the 15 countries for which comparison can be made is lower than one would have expected from a casual glance at the Table. In fact, r is only −0.22, which cannot be regarded as significant. Inspection shows that two countries are quite exceptional: Portugal with a rate of 703 in 1902 (as compared with 958 for Spain), while the rate of decline is relatively very low—namely, 40%. On the contrary, the rate for Northern Ireland was exceptionally high in 1901 and the rate of decline also high, at 75%. Eliminating these two countries, $r = -0.62$, which would be regarded as significant ($0.02<P<0.05$, 13 pairs) of inverse relationship between the two phenomena if it were not achieved by the more than dubious statistical expedient of eliminating cases unfavourable to the thesis. Apart from statistical techniques, however, it remains generally true that in the most advanced countries the percentage declines have been greatest, for reasons which are fairly obvious.

It is unnecessary to point out that this is most remarkable. In other classes of statistics one usually finds a tendency towards uniformity—that is to say, that statistics which were at variance in the past tend towards equality in the present. It is just the opposite with the young adult death rate. Fifty years ago (column 6) the range of variation was only from 958 (Spain) to 592 (Denmark), a ratio of less than 2:1, whereas the range is now nearly 3:1. Tuberculosis is no longer a problem in Denmark and the Netherlands. Perhaps the most important conclusion to be drawn is that in all Western countries the reduction of the death rate at young adult ages to a small fraction of even the present low rates in the most advanced countries may be attained in a short term of years.

Standard of Living and Mortality Rates

It has been established that there is a close relationship between socio-economic class and mortality rate. This is particularly notable in the case of tuberculosis, but it is also true of the general mortality rate. It might accordingly be expected that, comparing country with country, a significant negative correlation would be found between the

TABLE I.—*Death Rates per 100,000 Population per Annum in Certain Countries at Ages 15–44 in the Years 1899–1902 and 1947–9, and Derived Statistics. (Rates are standardized; generally they are simple averages of the rates in six quinquennial age groups)*

Country	Death Rates per 100,000 per annum												Percentage Decline (in all Causes) 1899–1902 to 1947–9			Males as % of Females 1947–9	Tuberculosis as % of Total 1947–9		
	All Causes						Tuberculosis (All Forms) 1947–9			All Causes Excluding Tuberculosis 1947–9									
	Males		Females		Persons														
	1899–1902	1947–9	1899–1902	1947–9	1899–1902	1947–9	M	F	P.	M	F	P.	M	F	P.		M	F	P.
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)
England and Wales (1901 and 1949)	702	210	588	178	645	194	51	54	52	159	124	142	70	70	70	118	24	30	27
Scotland (1900–1 and 1949)	820	271	753	274	786	273	82	115	99	189	159	174	67	64	65	99	30	42	36
Ireland (6 counties) (1901 and 1949)	870	244	985	216	927	230	67	69	68	177	147	162	72	78	75	113	27	32	30
Ireland (26 counties) (1901 and 1949)	838	297	805	318	822	307	119	137	128	178	181	179	65	60	63	93	40	43	42
Germany (1900–1 and 1949)	710	281	635	189	672	235	59	37	48	222	152	187	60	70	65	149	21	20	20
Denmark (1901 and 1949)	617	184	567	145	592	164	18	18	18	166	127	146	70	74	72	127	10	12	11
Spain (1900–1 and 1948)	987	528	930	370	958	449	183	129	156	345	241	293	47	60	53	143	35	35	35
Finland (1900–1 and 1949)	829	450	785	270	802	360	167	122	144	283	148	216	45	66	55	167	37	45	40
France (1901 and 1949)	863	294	758	213	810	254	74	55	65	220	158	189	66	72	69	138	25	26	26
Italy (1900–1 and 1949)	705	235	770	192	738	213	57	47	52	178	145	161	67	75	71	122	24	24	24
Norway (1900 and 1948)	867	213	727	141	796	177	65	49	57	148	92	120	75	81	78	151	31	35	32
Sweden (1900–1 and 1947)	697	226	657	191	677	208	60	64	62	166	127	146	68	71	69	118	27	34	30
Netherlands (1899–1900 and 1949)	617	200	605	126	611	163	22	20	21	178	106	142	68	79	73	159	11	16	13
Portugal (1902 and 1949)	753	494	633	347	703	420	224	147	185	270	200	235	34	45	40	142	45	42	44
Switzerland (1900–1 and 1949)	738	229	693	158	716	193	35	31	33	194	127	160	69	77	73	145	15	20	17
Iceland (1949)		236		129		183	39	32	36	197	97	147				183	17	25	20

Principal source of basic statistics from which this table was compiled: *W.H.O. Epidemiological and Vital Statistics Report*, Vol. III, Nos. 2–3.

national standard of living and mortality at young adult ages. Unfortunately the assessment of comparative average standards of living in different countries is beset with difficulties, statistical and other. Statisticians have produced statistics of national income and expenditure in the national currencies, and these statistics have much the same scope. The difficulty arises in establishing comparative costs for given quantities of given qualities of goods consumed and services utilized. It is definitely not good enough simply to convert to a common basis (say to £ sterling) national income in national currencies using rates of exchange, though this has been done by people who should know better, myself amongst the number for the present paper. Average national standards of living have also the well-known defects of averages when they cover too wide a range. If very great wealth were concentrated in the hands of a very few people, the generality of the population being poor, the average national income would tend to be misleading in its present application. This is not markedly the case, however, with the countries shown in Table I.

Before the war the rates of exchange were probably a much better indication of relative purchasing power of money than they are to-day. For this reason it has been thought advisable to compare the national standards of living in the different countries in 1938 instead of in 1948–9. It has been possible to derive national income per head, expressing £ sterling for 1938, for 12 of the 16 countries listed in Table I. The coefficient of correlation between the average standard of living in 1938 (as defined) and the general mortality rate for young adults in 1948–9 was found to be $r=-0.66$ and the correlation between the standard of living and the tuberculosis mortality rate was $r=-0.62$. Both of these are significant, for $0.02<P<0.05$ for 12 pairs.

Given the statistical imperfection of the measure of relative standard of living, one is probably entitled to assume that if a more exact and comprehensive measure were available the correlation would be even more decisive of the conclusion that, as between European countries, the higher the standard of living the lower the general death rate and the tuberculosis death rate amongst young adults. The best statistical techniques are no substitute for common sense and common knowledge; but here, surely, the statistical conclusion is just what one would expect. The higher the standard of living, whether between countries, within countries, or in a given country over time, the better the general welfare and all that pertains to it, including more and better food, better education, more and better hospital and medical services generally, better housing, better standards of sanitation—all of which must result in better health. The relationship, however, does not apply to each country separately: the death rates for Italy especially are far lower than the Italian national income would lead one to suppose: probably the Italian climate has much to do with this statistical aberration. In Ireland the general death rates at ages 15–44 are about 13% higher than they should be on the basis of national income alone; in England and Wales the excess is about 8%. Without overworking a theory, and not for a moment suggesting that other causes are not at work, the relative standards of living in the two countries can be regarded as "explaining" the greater part of the difference between them. As regards tuberculosis, however, the rates in both countries are much higher than they should be on this basis, in Ireland by about 50% and in England and Wales by about 40%.

The fact of the inverse relationship between death rates and average standard of living, as well as the probability that during the past 50 years the decline in the general young adult mortality rate is most marked in the more advanced countries, raises a question of crucial importance—namely, what proportion of the national resources should be *directly* devoted to the improvement of the general health of the community and a lowering of the death rate, and what proportion should be devoted to income-producing capital formation which is a prerequisite to improvement in the standard of living, having regard to the fact that such improvement in economic status will be conducive to a lowering of the death rate? Most countries are poor countries, which means that the total of resources available to the community for capital formation for health and other purposes is limited. The question posed is not a rhetorical one. Statistics cannot furnish an answer, because, even if the public authority has the power to deflect capital resources, decision on how much should be expended in the great divisions of income-producing capital formation on the one hand and into forms of capital which are not directly income-producing involves the balancing of economic and social values in a particularly acute, almost poignant, form when human life is involved. Economic values are usually measurable by statistics; non-economic social values are usually not so measurable. Every death of a young person is a tragedy, and most people closely affected by such a death would willingly have sacrificed all their income and their capital if the life could have been saved.

Causes of Death

For 10 groups of causes of death, the mortality rates per 100,000 population are displayed in very summary fashion for the different divisions of these islands in Tables II and IV and in Diagram III. Causes 1–9 are more or less specific and the drag-net heading 10 includes 19–26% of the numerically less important causes, in regard to which I must be content to refer you to the Reports of the Registrars-General.

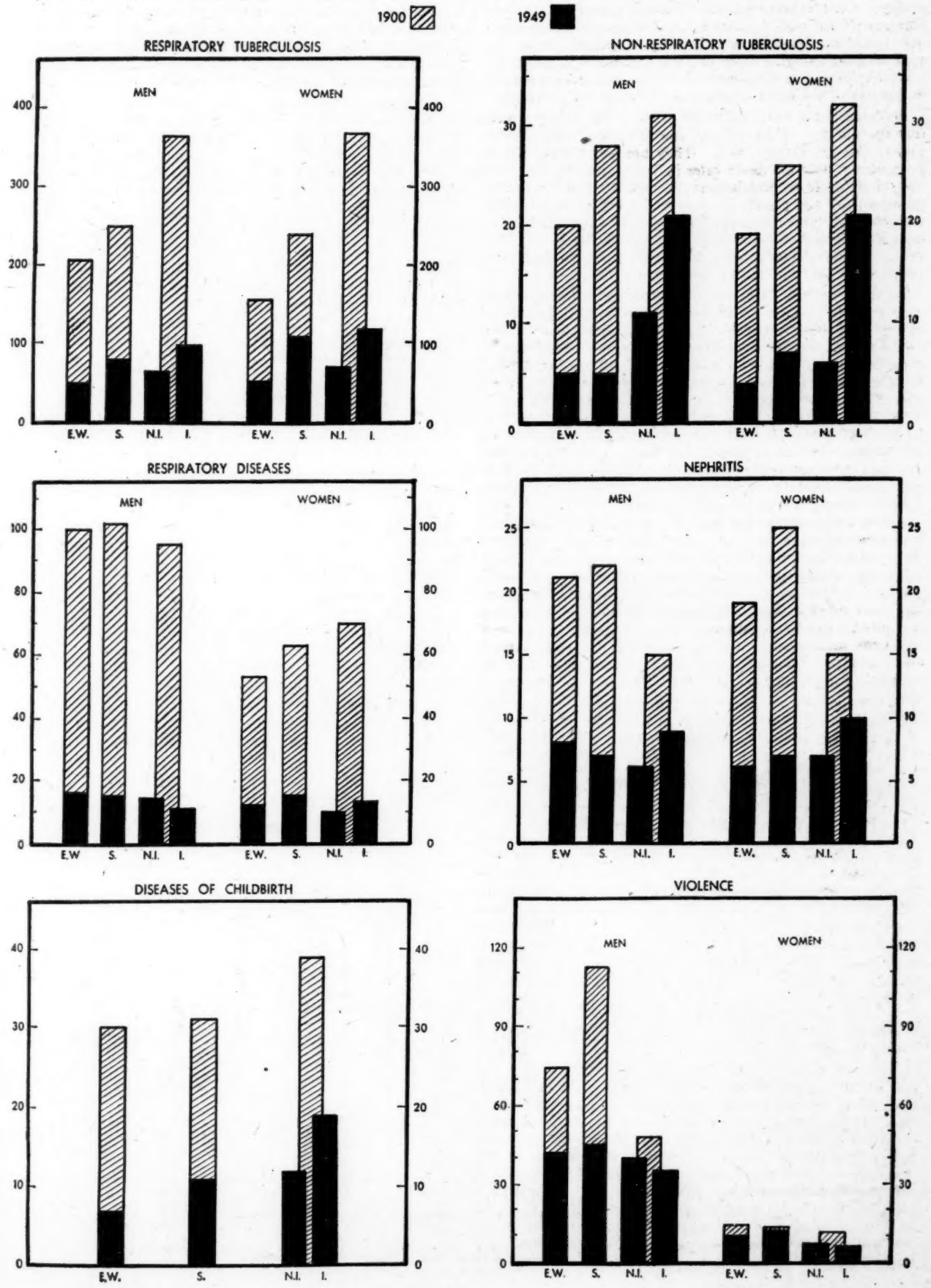
TABLE II.—*Crude Death Rates (per 100,000 population) in 1900, 1938, and 1949 in England and Wales, Scotland, Northern Ireland, and Ireland, Classified by Cause of Death*

Causes of Death and Year	Males				Females			
	E. & W.	Scotland	N. Ireland	Ireland	E. & W.	Scotland	N. Ireland	Ireland
1. Tuberculosis (respiratory system):								
1900	205	249	362		156	239	365	
1938	72	74	105	134	67	75	107	151
1949	48	77	62	96	50	107	68	117
2. Tuberculosis (all other forms):								
1900	20	28	31		19	26	32	
1938	9	13	19	27	7	13	21	31
1949	5	5	11	21	4	7	6	21
3. Malignant neoplasms:								
1900	15	14	11		30	26	21	
1938	21	21	21	15	30	30	24	25
1949	25	27	23	19	30	33	31	27
4. Diseases of the heart*								
1900	22	49	14		23	59	16	
1938	30	33	42	32	33	36	45	40
1949	26	32	28	33	21	29	31	33
5. Diseases of respiratory system:								
1900	100	102	95		53	63	70	
1938	34	45	36	37	18	21	25	31
1949	16	15	14	11	12	15	10	13
6. Nephritis:								
1900	21	22	15		19	25	15	
1938	10	12	13	12	10	12	12	15
1949	8	7	6	9	6	7	7	10
7. Diseases of childbirth:								
1900					30	31	39	
1938					19	36	46	37
1949					7	11	12	19
8. Suicide:								
1900	13	8	4		5	2	2	
1938	12	9	7	4	7	6	2	2
1949	9	5	5	3	5	3	2	1
9. Other violence:								
1900	61	104	44		9	11	9	
1938	48	57	31	26	9	9	6	7
1949	33	40	35	32	5	9	5	5
10. All other causes:								
1900	240	210	263		231	231	279	
1938	82	94	103	109	68	86	101	103
1949	49	57	63	61	41	52	49	59
11. All causes:								
1900	697	786	839		575	713	848	
1938	318	358	377	396	268	324	389	442
1949	219	265	247	285	181	273	221	305

* In 1900 the figures shown for diseases of the heart include endocarditis, valvular disease, pericarditis, hypertrophy of heart, angina pectoris. It is not possible to obtain figures comparable with those for 1938 and 1949, as diseases of the heart and of the circulatory system are grouped under the heading "diseases of the circulatory system," and it is not possible to separate the residual group "other and undefined diseases of heart or circulatory system" into heart diseases and diseases of the circulatory system. Compared with 1938 and 1949 the figures for heart diseases are understated.

DIAGRAM III

DEATH RATES BY CAUSES PER 100,000, 1900 AND 1949



Attention is directed to the footnote to Table II. Since 1900 the list of causes of death has been revised on a number of occasions, always in the direction of greater precision, concomitant with the development of medical science. Certification of cause of death is now much more accurate than it was 50 years ago. Comparisons of present-day rates, even when very broadly classified, as in the appended tables, with those of 1900, are accordingly somewhat hazardous, a qualification which attaches especially to diseases of the heart, for reasons stated in the footnote.

In Table II the death rates are crude—that is, they represent the quotient (×100,000) of the total deaths by population in the age group 15–44. They are accordingly not to be confused with the death rates in Table I, which, in effect, are standardized to populations of equal numbers in the six quinquennial age groups in the total span of years. The incidence of tuberculosis (all forms) has been briefly discussed in connexion with the analysis of Table I. In other tables the particulars for the respiratory and non-respiratory forms of the disease are shown separately.

Of the nine specific causes of disease shown, declines are recorded generally in all four regions except in the case of cancer and heart disease. The death rates in 1949 for women from *respiratory tuberculosis* are in all cases greater than for men. The death rates for Ireland are higher than for the other three areas for both men and women; actually the rates are twice as high as for England and Wales. In 1949 the rates were only about a quarter of what they were at the beginning of the century for men and about one-third for women: it will be noted that the declines were greater for men than for women. Not only has the mortality from the disease greatly declined but deaths from respiratory tuberculosis as a proportion of deaths from all causes have declined uniformly in the case of men. It is satisfactory to note that between 1949 and 1951 deaths from respiratory tuberculosis in Ireland at all ages have fallen by 22%.

Ireland makes an unsatisfactory showing as regards *non-respiratory tuberculosis*. The decline since 1900 has been far less than is the case with respiratory tuberculosis and the rate is four to five times that for Great Britain. In Denmark (with a larger population than Ireland) the actual number of deaths in 1949 from this disease at ages 15–44 was 28: in Ireland it was 260.

In all four regions *cancer* is on the increase, and the rates for women are higher than for men. It is rather remarkable, however, that in England and Wales the rate for women has been more or less stable since the beginning of the century. It will not be necessary here to discuss the reality of the increase (that is, whether or not it is due to more accurate certification) except to remark that in the age group under review in Ireland the rates are more reliable than at later ages because, in rural areas, the number of uncertified deaths, with consequent inaccuracy of statement of cause of death, is still quite large. Most of the deaths from cancer in the age groups reviewed are at ages 35–44.

As regards *heart disease* Ireland shows a marked tendency to increase. The Irish rates were in fact much below those of Great Britain at the beginning of the century, whereas they are now rather higher. As the footnote to Table II indicates, the rates for 1900 are understated to an unknown degree as compared with those for later years shown.

In all regions the most spectacular declines have been recorded in mortality from *diseases of the respiratory system*, though here again the declines are greater for men than for women. The rates are now but a small fraction of their level in 1900, and the Irish rates compare favourably with those for the other regions.

As regards *nephritis* the rates generally are less than half what they were at the beginning of the century. The Irish rates, lower than the British rates in 1900, are now somewhat higher.

While rates for *diseases of childbirth* are now much below their levels of 50 years ago—the decline since pre-war being notable—the Irish rate in 1949 was much higher than the rates for Great Britain.

While the rates for *suicide* in Ireland are based on only a few deaths, there is no doubt that they are significantly lower than the British rates. The rates for men are uniformly higher than those for women. Despite what we hear of the stress and strain of modern life, the recent decline in Great Britain is the more remarkable and may well be related to the extension of social security. The England and Wales male rate of 9 per 100,000 population in the age group 15–44 compares favourably with Denmark 35, Finland 33, Switzerland 29, Germany 22, and Sweden 20. These latter rates are a melancholy reflection on our modern civilization. Denmark's actual number of male suicides in 1949 at ages 15–44 was 319, as compared with Ireland's 22.

The death rate from *other violence* is very much greater for men than for women. It may come as a surprise that,

TABLE III.—*Age-specific Death Rates, England and Wales and Ireland, 1871–80 to 1949*

Area and Period	Males					Females				
	15–19	20–24	25–34	35–44	Total* 15–44	15–19	20–24	25–34	35–44	Total* 15–44
	Deaths per 100,000 population									
England and Wales:										
1871–80	525	736	934	1,380	982	545	681	861	1,160	878
1901–10	309	418	557	915	612	289	350	474	753	516
1921–30	262	341	386	634	440	248	302	345	485	368
1938	201	273	287	453	326	171	225	251	356	268
1947	162	205	212	344	246	121	182	194	274	206
1948	130	154	187	315	215	112	156	177	245	185
1949	127	159	175	312	210	96	143	165	248	178
Ireland:										
1871–80	508	732	888	1,076	861	519	608	806	965	778
1901–10	412	632	844	948	771	507	598	780	938	757
1921–30	321	492	533	708	549	371	484	561	745	578
1938	255	291	415	567	418	290	342	474	590	460
1947	207	295	367	556	391	252	370	379	489	393
1948	182	267	326	444	332	213	301	361	429	349
1949	155	232	266	431	297	140	250	331	428	318
	Percentage									
England and Wales, 1949 as percentage of:										
1871–80	24	22	19	23	21	18	21	19	21	20
1901–10	41	38	31	34	34	33	41	35	33	34
1938	63	58	61	69	64	56	64	66	70	66
Ireland, 1949 as percentage of:										
1871–80	31	32	30	40	34	27	41	41	44	41
1901–10	38	37	32	45	39	28	42	42	46	42
1938	61	80	64	76	71	48	73	70	73	69

* Standardized on basis of equal populations in each quinquennial age group.

despite the increase of deaths on the road, the rates for men for Great Britain were much lower in 1949 than in 1900 and even than in 1938.

As regards *all other causes* the great declines since the beginning of the century are a reminder of the virtual disappearance of infective and parasitic diseases (except tuberculosis), especially of typhoid fever, and the great decrease in diseases of the nervous system.

Ages at Death

Because of limitations of space I shall have to be content to do little more than let the relevant Tables III and IV and Diagram IV speak for themselves. Table III shows that in the short space of two years from 1947 to 1949 spectacular declines in death rates have been recorded in all age groups in England and Wales and in Ireland; during this period the declines were greater in Ireland than in England and Wales. That the end is not yet is indicated by the fact, already recorded, that between 1949 and 1951 the number of deaths from tuberculosis in Ireland at all ages, but specially affecting the young adult mortality, has fallen from 2,712 to 2,107, or by 22%. The position, in fact, is changing so rapidly that it is difficult to pinpoint it at any year. The death rates in 1949 in each age group and for each sex were substantially higher in Ireland than in England and Wales: the Irish rates in 1949 were generally at about the English level in 1938.

Low as were the English rates in 1938, the figures at the foot of Table III show that, as regards men, the percentage declines since 1938 are generally greater in England and Wales than in Ireland. There is, however, some indication that, within the general age group 15–44, the declines in Ireland in more recent periods are greater in the lower age groups than in the higher. This is what one would expect, but, remarkably, it does not appear to be the case in England and Wales except in a certain degree since 1938. Since 1921 there is but one exception in England and Wales to the rule that the female death rate is lower than the male; while there are some exceptions, the general picture is the reverse in Ireland. Over the whole period since 1871–80, the decline by 1949 in rates in England and Wales to about one-fifth of their level in the decade 1871–80 is quite uniform between the age groups. This is also evident from Diagram IV.

DIAGRAM IV

ANNUAL AVERAGE DEATH RATES PER 100,000 IN AGE GROUPS IN ENGLAND & WALES, 1871-80 TO 1949

(LOGARITHMIC SCALE)

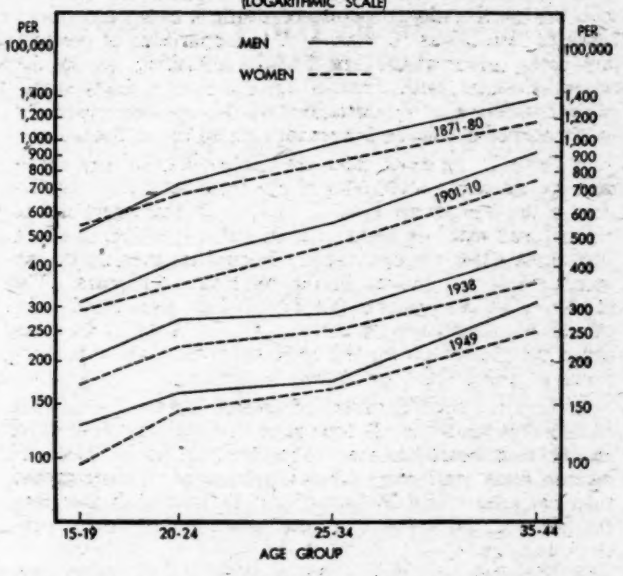


TABLE IV.—*Death Rates (per 100,000 population) in 1949 in England and Wales, Scotland, Northern Ireland, and Ireland for Each Cause of Death, Classified by Age*

Cause of Death and Country	Males			Females		
	15–24	25–34	35–44	15–24	25–34	35–44
1. Tuberculosis (respiratory system):						
England and Wales	29	51	60	53	62	35
Scotland	55	83	94	129	143	53
Northern Ireland	37	54	89	60	77	57
Ireland	69	116	111	99	151	102
2. Tuberculosis (all other forms):						
England and Wales	7	4	4	6	4	3
Scotland	6	5	3	14	4	3
Northern Ireland	8	10	14	5	5	8
Ireland	27	19	14	29	20	11
3. Malignant neoplasms:						
England and Wales	7	14	50	4	16	65
Scotland	6	16	62	4	20	76
Northern Ireland	3	12	57	4	14	79
Ireland	4	9	52	2	17	73
4. Diseases of the heart:						
England and Wales	9	15	48	8	16	36
Scotland	13	20	67	10	30	47
Northern Ireland	13	9	65	17	30	43
Ireland	10	23	74	12	30	63
5. Diseases of respiratory system:						
England and Wales	8	10	26	6	9	19
Scotland	7	10	28	7	14	24
Northern Ireland	2	11	31	6	7	16
Ireland	7	10	19	6	12	24
6. Nephritis:						
England and Wales	5	7	10	4	5	9
Scotland	3	7	12	5	4	12
Northern Ireland	4	6	9	6	6	9
Ireland	6	8	13	7	9	16
7. Diseases of childbirth:						
England and Wales				4	10	7
Scotland				6	16	11
Northern Ireland				3	13	22
Ireland				2	28	29
8. Suicide:						
England and Wales	5	8	13	2	5	8
Scotland	3	5	8	1	5	5
Northern Ireland	2	3	10	4	—	3
Ireland	1	3	7	1	1	3
9. Other violence:						
England and Wales	41	29	30	7	4	5
Scotland	41	39	41	10	7	9
Northern Ireland	30	39	25	4	6	3
Ireland	30	29	37	5	5	5
10. All other causes:						
England and Wales	33	37	71	27	33	62
Scotland	30	45	100	27	44	84
Northern Ireland	37	48	101	30	44	69
Ireland	39	49	106	29	58	101
11. All causes:						
England and Wales	144	175	312	121	165	248
Scotland	164	230	415	213	287	324
Northern Ireland	136	191	400	139	201	310
Ireland	193	266	431	193	331	428

Table IV shows that, apart from the general increase in the death rates with age (see also Diagram IV), there are marked divergences in the rates for main causes of death. Thus while the pulmonary tuberculosis rate was highest in 1949 for *women* in all four areas at ages 25–34, in Ireland alone this was true for *men*: in the other three areas the rate increased with age. Other forms of tuberculosis have generally their heavier incidence at ages 15–24. As already stated, deaths from cancer at young adult ages are practically confined to the ages 35–44. All the other diseases shown, except diseases of childbirth and violence other than suicide, increase with age. As regards diseases of childbirth, the age incidence is obviously related to age of mother at birth of child.

The material in Table IV can also be studied by expressing the death rates for each main cause as a proportion of death rates from all causes in each of the three age groups. From this point of view, in 1949 the incidence of respiratory tuberculosis was greatest for men in the age group 25–34 (when it accounted for 44% of deaths in Ireland) and for women in the age group 15–24 (in Scotland 61%, in Ireland 51%).

The first International Rorschach Congress decided in 1949 to publish a journal devoted to papers dealing with the Rorschach and other projective techniques for the study of personality. Hitherto such "Rorschachiana" had appeared in supplements to the *Schweizerische Zeitschrift für Psychologie*. The first number of the new quarterly journal, *Rorschachiana*, has now been published by Hans Huber, of Berne, at an annual subscription of 30 Swiss francs. Papers are published in English, French, German, or Latin.

AN INVESTIGATION INTO THE COMPARATIVE EFFICACY OF CERTAIN INHALANTS IN THE TREATMENT OF ASTHMA

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An investigation has been carried out at the Asthma Clinic, St. David's Hospital, Cardiff, into the efficacy of various inhalants commonly used in the treatment of asthma. This was prompted by the desire to have statistical information upon which to base advice to doctors and patients rather than to rely on the more prevalent but less scientific clinical impressions. The inhalants used and their costs are as follows :

	Hospital Price per fl. oz.	Retail Price per fl. oz.
	s. d.	s. d.
"Riddobron"	11 5	17 0
"Brovon"	8 0	13 6
"Neo-epinine" No. 2	9 6	15 9
Neb. adrenal. et atrop. co. (*N.F.*)	1 1½	3 6
A control mixture of water and glycerin 15%		

An indication of the cost to the hospital services is given by the fact that the cost of inhalants for one year was £260 for two Cardiff hospitals.

Method

Nineteen patients were selected to take part in the investigation ; their asthma had been fairly constant. All except two had previously used inhalers. The investigation began on October 3, 1950.

The solutions to be tested were supplied in small bottles, identified by letters, A, B, C, D, E, F, G, H, and I. The bottling and labelling were performed by the pharmacist at St. David's Hospital, and he alone knew the key to the contents of the bottles. The key was:

Riddobron	A and F
Neo-epinine No. 2	B and G
Brovon	C and H
Neb. adrenal. et atrop. co.	D and I
Control	E

The arrangement of the experiment initially was that each patient should use the five inhalants A, B, C, D, and E for one weekly period each. The patients were divided into five groups, and each group was given a different inhalant for the first weekly period. For the next four periods each group was issued with the inhalants next in alphabetical order. Thus one group was issued with the inhalants in the order A, B, C, D, and E ; another in the order B, C, D, E, and A, and so on. This procedure was adopted to minimize external influences, such as the weather, on the testing conditions for any one inhalant.

After the first five periods, when all the inhalants had been used by each patient, the patients were reissued with the inhalants (except the control), but in different orders and under new labels. For this part of the investigation the patients were divided into two groups, one group using the inhalants in the order G, I, F, and H, and the other in the reverse order. The patients were not informed that the same inhalants were being used. By this means a direct comparison, in successive weeks, of all the inhalants except the control was possible. During the first five weeks a control mixture was used, but in 16 out of 17 cases it was regarded as giving incomplete or no relief, and in some cases had to be given up. Its use was therefore discontinued, for the object of the investigation was to examine the comparative, and not the absolute, values of the inhalants.

Patients were normally seen at weekly intervals, and at each visit were given a supply of different inhalant and a card upon which to record the number of times the inhalant was used during each 12 hours for the period, any other treatment found necessary, and any untoward happenings which might have affected them. Patients were instructed that if they were unable to attend in one week they should continue using the inhalant issued and attend the next week. They were asked to discontinue using any particular inhalant only if attacks were quite uncontrolled by it or if it was too unpleasant to use.

At each visit the patient's assessment of the relief obtained from the inhalant just used ("good," "incomplete," or "no relief") and the incidence of side-effects were recorded. Inquiries were made regarding any alteration in his health or normal routine and its effect on his asthma.

The patient's comparison of the inhalant with the previous one used was recorded as "better," "worse," or "same." In making the comparison the criteria used were the speed of action, the frequency of use, the degree of relief, the side-effects experienced, and the amount of other symptomatic treatment required ; all these factors were taken into account by the patient. Alterations in asthmatic states were also considered. If, for example, a patient's asthma was worse during one period and an inhalant had to be used more often than that in the next period, he might still prefer the former, making due allowance for his condition.

The survey began with 18 patients, and one joined during the third week of the survey. Not all were able to complete the full course of inhalants ; 12 used all the inhalants, one used eight, one used seven (although issued with eight), one used six, three used five, and one used four. Table I shows the number of periods each inhalant was used and the number of patients who used each inhalant for two periods, under different labels. Thus six patients used riddobron as A and 13 used it once as A and later as F.

TABLE I.—*Number of (weekly) Periods Each Inhalant Used*

	Riddobron	Neo-epinine No. 2	Brovon	N.F. Mixture	Control
No. of patients using inhalant for 2 periods ..	13	15	12	15	0
No. of patients using inhalant for 1 period ..	6	4	7	4	17
Total periods used ..	32	34	31	34	17

Results : (1) Comparative Assessment of the Inhalants

The inhalants, except the control, were all used on successive weeks and a direct comparison was made possible.

Table II shows which pairs of inhalants were used on successive weeks by each patient and the preference of the patient. The Table is not chronologically arranged and does not show the order in which the inhalants were used. The paired names at the top indicate the inhalants compared, and the names in the columns underneath which of the inhalants were preferred ; the letter O indicates that the patient had no preference and thought them equally good or bad. The total at the foot of each column shows the number of times each pair of inhalants was compared. Thus in the comparison of riddobron and neo-epinine No. 2, which was made 16 times, riddobron was preferred on four occasions, neo-epinine No. 2 on 11 occasions, and on one occasion no preference was made.

TABLE II.—*Results of Comparing Inhalants on Successive Weeks*

Case No.	Ridd./Neo-ep.	Neo-ep./Bro.	Bro./N.F.	Ridd./Bro.	Ridd./N.F.	Neo-ep./N.F.	Ridd./Cont.	N.F./Cont.
1	Neo-ep.	Bro.	Bro.	Bro.	N.F.	O	—	N.F.
2	,,	—	,,	,,	O	O	O	,,
3	,,	O	,,	Ridd.	Ridd.	Neo-ep.	Ridd.	—
4	—	Neo-ep.	N.F.	Bro.	N.F.	,,	,,	N.F.
5	Neo-ep.	—	Bro.	Ridd.	Ridd.	O	,,	,,
6	Ridd.	Bro.	,,	,,	N.F.	Neo-ep.	—	Cont.
7	O	,,	—	O	Ridd.	N.F.	Ridd.	N.F.
8	Neo-ep.	Neo-ep.	O	Bro.	O	,,	,,	—
9	,,	—	N.F.	Ridd.	N.F.	,,	,,	N.F.
10	Ridd.	Bro.	Bro.	Bro.	O	Neo-ep.	—	Cont.
11	Neo-ep.	,,	—	,,	Ridd.	,,	Ridd.	N.F.
12	—	Neo-ep.	N.F.	Ridd.	,,	,,	,,	,,
13	—	O	O	—	O	O	,,	,,
14	Ridd.	Neo-ep.	—	—	—	N.F.	,,	,,
15	Neo-ep.	O	—	—	—	O	—	—
16	,,	Bro.	N.F.	—	—	—	Ridd.	—
17	Ridd.	Neo-ep.	,,	—	—	—	,,	—
18	Neo-ep.	O	—	—	—	—	,,	N.F.
19	,,	Neo-ep.	N.F.	—	—	—	—	—
Total ..	4 Ridd. 11 Neo-ep. 1 O	6 Bro. 6 Neo-ep. 4 O	6 Bro. 6 N.F. 2 O	5 Ridd. 6 Bro. 1 O	5 Ridd. 4 N.F. 4 O	4 N.F. 6 Neo-ep. 5 O	13 Ridd. 1 O	2 Cont. 11 N.F.
	16	16	14	12	13	15	14	13

Abbreviations indicate which inhalant of each pair was preferred: O indicates no preference. Ridd. = Riddobron. Neo-ep. = Neo-epinine No. 2. Bro. = Brovon. N.F. = Neb. adrenal. et atrop. co. (*N.F.*). Cont. = Control, water and glycerin 15%. — = No comparison made.

TABLE III.—*Effectiveness of Inhalants*

	No. Periods Used	Relief			No. Times Discontinued
		Good	Incomplete	No Relief	
Riddobron	32	21	9	2	2
Neo-epinine No. 2 ..	34	24	9	1	1
Brovon	31	21	8	2	3
N.F. mixture	34	20	11	3	2
Control	17	1	5	11	4
Total	148	87	42	19	12

TABLE IV.—*Side-effects of Inhalants*

Inhalant	Total Periods Used	Periods Used with Side-effects	Dryness	Irritation	Taste	Cough	Nausea	Palpitation	Sneezing	Headache	Chest Pain
Riddobron ..	32	14	6	4	3	3	1	1	1	1	—
Neo-epinine No. 2	34	25	12	7	8	4	1	2	4	—	—
Brovon ..	31	20	8	10	7	5	3	—	1	1	1
N.F. mixture ..	34	20	7	10	10	4	—	2	1	—	—
Control ..	17	7	3	2	1	3	—	1	—	—	—
Totals ..	148	86	36	33	29	19	5	6	7	2	1

(2) Relief Obtained from the Inhalants

Table III shows the number of periods of one week each inhalant was used, the relief obtained, and the number of periods in which each inhalant had to be discontinued. In ascertaining the degree of relief the patient's impressions were used, as no satisfactory objective criteria could be found. Thus the time elapsing before relief is felt can vary from immediately to five minutes in different persons, all of whom may call the relief obtained from the inhalant good. Each inhalant was used about the same number of times, except the control, which was abandoned after the first five weeks.

It will be seen that inhalants were discontinued on 12 occasions, on each occasion due to insufficient relief being given, except one which was discontinued because of unpleasant side-effects. One patient discontinued riddobron, neo-epinine No. 2, brovon, and the neb. adrenal. et atrop. co., the latter on two occasions. He was a chronic asthmatic who had severe asthma. Riddobron was discontinued on another occasion by a patient who had a severe cold which worsened her asthma. She reverted to her usual brovon, but had to use that frequently. Brovon was discontinued on another occasion by a patient who suffered an exacerbation of his asthma during the period. On another occasion it was discontinued by a patient whose asthma was not worse than usual but who noted unpleasant effects. The control mixture was discontinued on four occasions. Three of the patients had their usual asthma on these occasions; the fourth had an exacerbation due to a superadded chest infection.

(3) Side-effects of the Inhalants

Table IV shows the side-effects obtained with these inhalants and the frequency with which they occurred. It will be seen that the control mixture gave rise to unpleasant side-effects on very few occasions. The other inhalants were used for 131 periods, for 79 periods with side-effects. The commonest side-effects seen were dryness, oral and pharyngeal irritation, unpleasant taste, and cough. Less common side-effects were nausea, palpitation, sneezing, headaches, and chest pain.

Table V shows the incidence of side-effects reported with each inhalant and the total number of side-effects reported with each inhalant. Thus, for example, riddobron was used for 14 periods when side-effects were recorded. In nine of these periods only one side-effect was reported, and in only one period were three side-effects recorded.

TABLE V.—*Showing Incidence of Side-effects with Each Inhalant*

	Riddobron	Neo-ep. No. 2	Brovon	N.F. Mixture	Control
No. periods used with side-effects	14	25	20	20	7
No. periods used with:					
1 side-effect	9	16	11	11	3
2 side-effects	4	5	4	4	2
3 ,, ,, ...	1	4	3	5	1
4 ,, ,, ...	—	—	2	—	—
Total side-effects	20	38	36	34	10

Table VI shows the number of periods the different inhalants were used without any side-effects being recorded and the degree of relief obtained during these periods. Thus, for example, it will be seen that riddobron was used for 32 periods; no side-effects were recorded in 18 periods: of these 18 periods good relief was obtained in 13, incomplete relief in four, and no relief in one.

TABLE VI.—*Effectiveness of Inhalants Used Without Side-effects*

	Total Periods Used	Total Periods Used with No Side-effects	Relief		
			Good	Incomplete	No Relief
Riddobron	32	18	13	4	1
Neo-epinine No. 2 ..	34	9	6	2	1
Brovon	31	11	7	2	2
N.F mixture ..	34	14	8	4	2
Control	17	10	1	2	7

(4) Comparison of Assessments of Inhalants

As a test of the patients' reliability and consistency in the assessment of the relief obtained from the inhalants, their assessments of the same inhalants used under different letters have been examined. The results are shown in Table VII.

TABLE VII.—*Comparison of Inhalants Used Under Different Letters*

Inhalant	No. Patients Who Used Inhalant Twice	No. Patients Giving Different Assessment	Reason for Difference	
			No Apparent Reason	Exacerbation of Asthma
Riddobron A and F	13	3	1	2
Neo-epinine No. 2 B and G ..	15	5	1	4
Brovon C and H..	12	6	3	3
N.F. mixture D and I	15	3	1	2
Totals ..	55	17	6	11

Thus riddobron was used twice (as A and F) by 13 patients. Three gave a different assessment when they used it a second time. With one patient there was no apparent reason for the difference. The other two had an exacerbation of their asthma when they gave a different assessment.

In connexion with the variation in assessment it is interesting to study the patients' assessment of their usual inhalants when they were used as unknown inhalants. Most patients had one usual inhalant, and two used two inhalants regularly. They all regarded their usual inhalants as being of great value and capable of affording good relief.

Six patients customarily used riddobron, and during the experiment five of them used it twice as A and F. Three of the five patients assessed the relief as good on both occasions. Two of the five assessed the relief as good on one occasion and incomplete on another during an exacerbation of the asthma. One patient used it once only, and assessed the relief as good.

Eleven patients customarily used brovon, and during the experiment eight of them used it twice as C and H. Three of the eight patients assessed the relief as good on both occasions. Five of the eight assessed the relief as incomplete on one occasion and good on another. On three of the "incomplete" occasions there was a worsening of the asthma; on one there was no apparent reason, and on the last the patient actually discontinued using the inhalant as C because of lack of relief and reverted to his own brovon. When he used brovon as H he gave it a good assessment. The remaining 3 of the 11 patients used brovon as C. One found the relief good, another incomplete (for no apparent reason), and the third discontinued the inhalant owing to lack of relief and reverted to his own brovon.

(5) Study of Frequency of Use of Inhalants

Patients recorded on a card the number of times they had recourse to each inhalant during every 12-hour period—9 a.m. to 9 p.m. and 9 p.m. to 9 a.m. In some cases no record was submitted for the 12 hours in which the clinic was visited and the inhalant changed. Because of this the index "the average number of times used per 12-hour period in each week" was calculated (*a*) for day periods, and (*b*) for night periods.

The patients were unaware that inhalants A and F, B and G, C and H, and D and I were the same, so that the records giving the number of times F was used may be regarded as replications of records of A. Similarly, G records are replications of B, H of C, and I of D.

Four average values were therefore provided by each patient in regard to each inhalant—namely, the average number of times inhalant A was used per 12-hour *day* period, and also per 12-hour *night* period; and replications of these two averages when the same inhalant (F) was, unknown to the patient, used. Excluded from the primary tabulation of these averages (Table VIII) were all instances

TABLE VIII.—*The Average Number of Times Each Inhalant was Used per 12-hour Period (Over a Week), Together with the Total Times per 48-hour Period*

Patient	Inhaler AF					Inhaler BG				Inhaler CH				Inhaler DI				Total	Total + Estimated Missing Numbers
	Day	Night	Day	Night	Total	Day	Night	Total		Day	Night	Total		Day	Night	Total			
1	11·429	6·571	7·429	5·429	30·858	9·429	7·571	32·428		8·286	6·429	25·715		8·143	6·571	31·428		120·429	4·715
2	0·143	0·429	—	—	0·572	0·143	0·429	2·858		8·857	6·571	0*		0·143	0·571	1·285		4·715	
3	1·286	3·143	0·571	2·429	7·429	1·286	3·286	9·572		—	2·286	11·929		1·714	3·143	9·857		38·787	
4					6·820*	0·286	1·143	5·144		1·857	3·143	3·000		1·714	4·143	7·857		16·001	22·821
5	8·429	4·286	8·000	4·000	24·715	7·571	4·000	23·428		0·429	3·286	21·856		7·143	4·143	23·572		93·571	
6	1·857	5·429	1·571	4·286	13·143	1·429	3·714	14·000		3·000	5·857	14·000		2·571	5·429	16·429		57·572	
7	0·143	0·286	0·429	1·000	1·858	0·857	0·143	1·715		0·286	0·429	3·190		0·714	0·143	2·143		8·906	
8	3·714	4·429	2·571	2·429	13·143	3·714	3·000	12·714		2·857	3·143	13·571		3·857	6·286	17·572		57·000	
9	7·857	1·571	8·857	2·714	20·999	8·000	1·000	20·857		8·714	3·143	18·286		8·857	1·143	20·142		80·284	
10	6·429	3·571	12·429	10·714	33·143	8·143	6·143	20·715		5·286	1·143	12·001		4·571	1·714	10·428		76·287	
11					26·007*	7·714	3·571	25·285		10·000	4·000	23·472*				24·805*		25·285	99·569
12	0·286	1·143	0·857	0·714	3·000	0·571	1·714	3·142		0·143	1·286	1·858		0·429	1·000	1·572		9·572	
13	6·571	6·286	7·429	3·571	23·857	6·143	6·714	20·571		3·714	4·000	19·428		7·857	6·857	20·999		84·855	
14	0·571	1·143	0·286	0·143	2·143	0·571	0·857	1·857		3·000	0·429	3·714		1·857	2·000	4·571		12·285	
15	1·750	2·250	0·286	0·429	4·715	1·286	2·857	7·286		2·143	0·857	2·678*		0·714	0·286	1·714		13·715	16·393
Totals ..	50·465	40·537	50·715	37·858	179·575	57·143	46·142	53·857		44·430	36·857	201·572		39·429	31·429	148·548		699·264	
Totals + estimated missing numbers					212·402			—				174·698				194·374			783·046

* Average times used per patient as estimated from missing plot technique (Kendall, 1946).

in which all four averages were not available for any specified inhalant. For example, patient No. 2 used inhalant C but not H, and was therefore excluded from the tabulated values of CH. Although some adjustment of this became necessary in the course of the analysis, a dash in the Table indicates that the patient was given the inhalant but had no occasion to use it during the week. In the result, 13 sets of four values were available for inhalant AF, 15 for BG, 12 for CH, and 14 for DI—a total of 54 sets of four averages for the four inhalants.

Combining the average values for each set of four gives the average number of times each inhalant was used by each patient during a 48-hour period. From these values the means for each inhalant per 48-hour period per patient were:

Inhalant	Average No. of Times Used per 48-hour Period
Riddobron	13·8
Neo-epinine No. 2	13·4
Brovon	12·4
Neb. adrenal. et atrop. co.	12·1

Whilst it is true that these differences between the inhalants are not large, they seemed sufficiently so to warrant a study of their statistical significance by an analysis of variance.

The total "sum of the squares" (of the deviations of the 216 individual readings from the grand mean of all readings) was 1962.115, with 215 degrees of freedom (Table IX).

TABLE IX

	D. of F.	Sum of Squares	Mean Square	F. Value	
				Calculated	Theoretical 1% Level
Between plots	53	1422·481	26·839	8·1	1·7
Within plots	162	539·634	3·331		
Total	215	1962·115			

It was convenient for this purpose to denote a set of four readings by one patient using one inhalant as a "plot," and since there were 54 such plots this gave 53 degrees of freedom between plots with sum of squares 1422.481, leaving 162 degrees of freedom within plots with sum of squares = 539.634. The variance ratio (F) 26.839/3.331 = 8.1 was significant, indicating that there was much greater variation between plots than within plots.

The usual procedure would next be to split up the sum of the squares *between* plots into the amount due to variation between patients, the amount due to variation between inhalants, and the amount arising from interaction of the two, giving in fact:

	Degrees of Freedom
Between patients	14
,, inhalants	3
Patients × inhalant interaction	42
	59

Here, however, the matter was complicated by the fact (noted above) that instances where all four readings were not available for any plot had been excluded. If differences between patients exist—as in fact will later be demonstrated—the missing values would not affect the inhalant totals equally. For this problem it seemed accurate enough to estimate the six missing plot values by the technique suggested by Kendall (1946) and to reduce the degrees of freedom for "patients × inhalant interaction" to 42 − 6 = 36 (see Table X).

For the purpose of splitting up the variation *within* plots (which is unaffected by the inclusion of the six estimated total plot values) it should be noted that there were three degrees of freedom within any one plot—namely,

Between replications	1
Within replications:	
Between night and day	1
Error	1

making for the 54 such plots together, the 54 × 3 = 162 degrees of freedom shown above. The analysis is shown in Table X.

Discussion of Analysis of Variance

All sources of variation examined in Table X are significant at the 1% level when tested against the residual variance (column 5), but the striking feature is the size of the

TABLE X.—*Analysis of Variance*

Source of Variation	D. of F.	Sum of Squares	Mean Square	Tested Against Residual Variance	Tested Against Interactions
Between plots:					
Between patients	14	1309·710	93·6	175·2*	
Between inhalants	3	12·162	4·1	7·6*	1·5 N.S.
Patients × inhalant interaction	36	100·609	2·8	5·2*	1·0
	53	1422·481			
Within plots:					
Between replications	54	158·903	2·9	5·5*	
Within replications:					
Between day and night (Day − Night) × plots interaction	1	19·919	19·9	37·3*	3·2 N.S.
	53	332·002	6·3	11·7*	1·0
Residual	54	28·810	0·534	1·0	
	162	539·634			
Total	215	1962·115			

* = Significant at 1% level. N.S. = Not significant.

mean square deviation between patients, giving a variance ratio of 93.6 ÷ 0.534 = 175.2 (F = 2.43). Thus there are great variations between the members of this group of patients as regards frequency of use of these inhalants which are not assignable to differences between inhalants, to differences between repeated use of the same inhalant (replications), or to differential usage during day and night. The significance of the mean square for interaction between patients and inhalants (2.8/0.534 = 5.2) indicates, as would be expected, that the effect of any specified inhalant is not always the same but depends on the patient by whom it is used.

The fact that the comparison of the mean square deviation for inhalants with the *residual* is significant (4.1/0.534 = 7.6) merely means that if a very much larger number of observations had been obtained *from these same 15 patients* there would have been real differences between the frequency of use of the four inhalants. But since, as shown above, inhalant effects vary from patient to patient, the problem to be solved is: although there are differences between the effects of inhalants among these 15 patients, is there any evidence that these differences would appear amongst the general population of asthmatic patients? The appropriate test is to compare the mean square deviation for inhalants not against the residual but against the mean square for interaction between patients and inhalants (4.1/2.8 = 1.5) (column 6 of Table X). This variance ratio is not significant even at the 5% level, and the conclusion must be that there is no evidence from these data that real differences would exist between the frequency of use of these four inhalants amongst the general population of asthmatic patients.

That great caution is needed in the interpretation of these differences between the frequency of use of the inhalants is further stressed by the fact that there is significant variation between the responses of these patients to the same inhalants on different occasions (replications).

It may also be noted that these 15 patients show significant variation in the frequency of day compared with night use, but again not to the degree that would justify the assumption that similar variation is present in the whole population.

The main conclusion from the analysis of variance is that, although some slight difference is apparent in the average frequency with which these 15 patients had recourse to the four inhalants, there is no evidence from the material

analysed to justify an assumption that similar real differences in the frequency of their use would occur in the general population of asthmatic patients. The effect of any one inhalant was found to vary greatly from patient to patient and on different occasions for the same patients.

Summary and Conclusions

An experiment was designed to compare the need for recourse to four inhalants—riddobron, brovon, neo-epinine No. 2, and neb. adrenal. et atrop. co. (*N.F.*)—and their effect on a series of asthmatic patients.

No outstanding degree of preference was expressed for any one inhalant, and only the control inhalant was specifically commented upon adversely (see Table II).

The proportion of the total weekly periods used, which resulted in "good relief," "incomplete relief," and "no relief," were similar for all inhalants (except the control inhalant) (see Table III).

There were slight differences between the average number of times each inhalant was used per twelve-hour period in each week, but the evidence was not strong enough to justify the conclusion that similar differences would exist amongst the general asthmatic population.

The use of all the inhalants (except the control mixture) was discontinued an approximately equivalent number of times, for various reasons.

Measured objectively by the frequency of use, there was significant variation between the responses of patients to the same inhalants on different occasions; this was reflected in the subjective assessments of the same inhalant at different times and the usual inhalant when used as an unknown.

Each inhalant was given a poor assessment by a proportion of patients.

There was no difference of statistical significance between the inhalants as regards the incidence of side-effects (Tables IV and V). The side-effects most commonly noted during the investigation were dryness of the mouth, oro-pharyngeal irritation, unpleasant taste, and cough. Table VI shows that pleasantness is not incompatible with effectiveness.

It would seem from this investigation that, of the four inhalants specified, not one is outstanding, whether judged subjectively according to patients' opinion or objectively according to recorded frequency of recourse to it. Also, it became apparent that, although some asthmatic patients strongly affirmed their preference for one particular inhalant, that was not solely on account of any intrinsic value the inhalant may possess. The opinion may not be so favourable if the inhalant is first tested at an inauspicious time. The cheapness of the neb. adrenal. et atrop. co. is not accompanied by a corresponding feebleness of action.

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ASTHMA IN CHILDHOOD

A SURVEY OF THE WORK OF AN ASTHMA CLINIC IN HAMPSHIRE

BY

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Over a period of many years I have been increasingly impressed by the number of patients presenting at the Royal Hampshire County Hospital with clear physical signs of the effects of asthma, which no systematic or continued attempt had been made to prevent. I was therefore prompted to initiate a special clinic for asthma and other allergic diseases, with the purpose of the systematic investigation and continued management of asthmatic children. After consultation with colleagues and with the county medical officer of health, the clinic was begun early in 1947.

One advantage of an asthma clinic is the progressive increase in the number of patients who attend from year to year: the mere presence of such a special clinic in an area brings to medical treatment sufferers who might otherwise be content to continue without treatment until their health was irrecoverably damaged. In this clinic we have now investigated, treated, and followed up 209 children of school age and under. This preliminary report shows something of the pattern of the natural history of asthma, as affected by treatment, in a predominantly agricultural but partly urban area in Southern England. Adults suffering from allergic conditions are also investigated and treated in the clinic, but are not here considered.

Age and Sex Incidence

The grouping of patients according to their age at the onset of asthmatic symptoms is shown in the accompanying Table. It will be seen that in 84% these symptoms appeared in the first seven years of life.

Age at Onset of Symptoms of Asthma

	Age in Years																Total
	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13	-14	-15	-16	
Boys	24	15	29	19	10	15	9	4	1	6	5	2	0	1	1	1	142
Girls	11	6	15	7	8	4	4	3	2	2	2	2	1	0	0	0	67
Total	35	21	44	26	18	19	13	7	3	8	7	4	1	1	1	1	209

Boys are affected more often than girls, in the proportion of 2:1 (142:67). Coke and Coke (1939), in 3,000 adult and child asthmatics, found only 8% more males than females, but they report that boys are affected more often than girls and show that the approach to equality in the overall figures derives from a preponderance of women between puberty and the menopause over men of the same age period. The Table shows the age of onset to be similar in boys and girls.

A definite history that a close relative had suffered from an allergic condition was obtained in 49% of our cases, a figure similar to that reported by Coke and Coke (1939) and Williams and Williams (1949).

Degree of Disability

Figures showing the average loss of school time are in course of collection, but their accumulation must necessarily be slow; on the one hand, not all the school time lost by asthmatic children is lost by reason of asthma, and, on the other hand, long periods of absence from school at a time antecedent to the diagnosis of asthma may be ascribed to some other cause. How great a handicap the

disease may be to a school-child is clearly shown by one girl patient who in three years lost 96 school days from asthma alone.

This sociological aspect of asthma is particularly important in the new educational system, which decides the future educational fate of a child by examination at the age of 11. The asthmatic child may by reason of his disability be excluded from a secondary education even though in fact the intelligence of a high proportion of asthmatic children is above average.

This effect on the education of the child would in itself be important enough to demand special attention, but there are other equally cogent reasons for a systematic attempt to make special arrangements for asthmatic children. Skeletal changes in the chest cage and spine arise chiefly in the first growing period—pigeon chest, kyphosis, kyphoscoliosis, contracted pectoral muscles, and round shoulders; and visceral effects—emphysema, fibrosis of lungs, bronchiectasis, right heart strain—inevitably lead to restriction of occupational opportunity and even to diminished expectation of life.

Associated Allergic Manifestations

The two commonest associated allergic manifestations were eczema and rhinitis, but in respect of rhinitis it was difficult to separate those cases which were purely allergic from those which were due to, or had an element of, upper respiratory infection.

Eczema.—Of the 209 cases, 57 (27%) suffered or had suffered from eczema. Of these 57, 35 were boys and 22 were girls; 33% of the girls and 24% of the boys had asthma and eczema coincidentally. The patients who suffered from both asthma and eczema could be grouped in two classes: those in whom the eczema had disappeared at about the age of 3 years, when they had cut the deciduous teeth; and those in whom the eczema persisted after the age of 3, or began after the age of 3, continuing sometimes into adult life. In 13 of 35 boys and in 19 of 22 girls eczema was present after the age of 3. Only 8 of these 13 boys and only 12 of these 19 girls had positive skin reactions. In 11 of these 13 boys in whom eczema persisted, exacerbations of the eczema and asthma did not occur together but alternated, but in only 6 of the 19 girls did the attacks behave in this way. It is difficult to express the distribution of the eczema in these cases mathematically in any detail. The commonest situations in the older children were the flexures of the elbows, wrists, and knees, and the fingers and toes; while in the younger children these areas were usually affected, and also the face, head, and neck. Two patients in the series, both of them boys, also suffered from urticaria.

Inheritance.—A definite history of a near relative who suffered from an allergic condition was obtained in 102 cases (49%)—a figure very close to that arrived at by Coke and Coke (1939) and Williams and Williams (1949). There were no significant differences in other respects between those who furnished a family history of allergic disease and those who did not.

Specific Skin Reactions.—Positive reactions were obtained in 106 children (51%). In some cases tests for specific skin reaction were repeated, but over the period under study the positive reactions did not become more numerous with increasing duration of the disease. By far the largest proportions of the positive reactions were associated with the inhalant groups, particularly feathers, down, horse-hair, and house dust. Only 16 children were sensitive to the pollen group, and most of these to grass pollen. Ragweed sensitivity, which bulks so largely in Gay's (1946) American series and which gives a high incidence in August and September, was not observed. One child was sensitive to milk protein.

Associated Chest Disease.—Clinical or radiological evidence of pulmonary disease other than emphysema was obtained in 21 patients (10.5%). Seven showed bronchiectasis, confirmed by bronchogram; four had calcified tuberculous foci; one proved to have active tuberculous infection; four showed increased hilar markings, one had bilateral cystic disease of the lung, one had lobular atelectasis, two had hilar fibrosis, and one showed changes interpreted as due to congestion. The proportion of cases showing increased hilar shadows is similar, but the proportion showing other organic disease in the lung is substantially higher than in the smaller Yorkshire series reported by Royle (1952).

Whooping-cough.—In 96 (65 boys and 31 girls) there were definite histories of whooping-cough. In only 19 of the boys and in only 5 of the girls did asthma coincide with or follow immediately after the attack of whooping-cough.

Other aetiological factors are reflected in the specific forms of treatment thought to be indicated by the results of our investigations.

Treatment

The continued risk to which the asthmatic child is subject over a period of many years, the degree in many cases of the ultimate disability, and the effect of the disease on his education and future employment make necessary the closest investigation of the patient and perhaps his prolonged management. This is best undertaken at a specialized clinic where a clinician responsible for the patient as a whole can have the co-operation of his specialist colleagues and of the family doctor. Treatment is seldom dramatic, and it is often difficult to retain the co-operation of the child and parents. Attacks continue to occur from time to time during treatment, inducing depression and a feeling of hopelessness, to combat which the most constant encouragement, optimism, and interest are essential.

Drugs.—Phenobarbitone in doses of ¼ or ½ gr. (16 or 32 mg.) according to age, once or twice daily, was prescribed for most of the patients and was continued for long periods. Many patients in addition were given antihistamine drugs such as mepyramine hydrogen maleate ("anthisan"), 50 mg. two or three times daily, diphenhydramine hydrochloride ("benadryl"), 25 mg. once or twice daily, or promethazine hydrochloride ("phenergan"), 10 mg. once or twice daily. Ephedrine, ¼ or ½ gr. (16 or 32 mg.), was given for the relief of actual spasm. The standard method of prophylaxis against attacks has been the regular administration of phenobarbitone, but children who are constantly wheezy receive ¼ or ½ gr. (16 or 32 mg.) of ephedrine regularly with the phenobarbitone. Where it seems suitable the mother is provided with ephedrine tablets, which she can give whenever an attack seems to be imminent.

Desensitization.—Children whose skin tests showed specific sensitivity were given courses of desensitizing injections if they were over 5 years of age. One child who was very sensitive to milk protein had this removed from her dietary, with a decrease in the severity and number of her attacks. In some cases feathers, pillows, eiderdowns, and other bedclothes were removed from the bed or from the immediate proximity of the child. Only with the highly allergic was any change made in the more distant furniture of the room. In this way it was hoped that in most cases a very high concentration of protein particles would be avoided in the air directly around the child, but in most cases it was felt undesirable to give the bedroom an abnormal appearance in case the child's feeling of invalidism should be increased. In children not highly allergic it was thought suitable to provide in this way a moderate concentration of varied protein material in the environment.

Treatment of Associated Nasal Disease.—Sixty of the children had had their tonsils and adenoids removed before being referred to the asthma clinic. A further 47 underwent tonsil and adenoid operations, being referred from the clinic to the ear, nose, and throat department. Forty children had antrum washouts and eight had other intranasal operations. In this group there is a certain amount of overlap, one child sometimes having more than one operation. Of 25 boys who had antral washouts 16 showed definite pus. Of eight girls similarly treated only four proved to have actual pus in the antrum. In the others the antrum was filled not with pus but by oedematous mucosa. All those children who

suffered from rhinitis were given decongestive drops. It is often argued that these drops may find their way to the bronchi and give rise to bronchial catarrh, but I have used them in children and adults for many years for the treatment of catarrhal and congestive conditions in the nose, and in no instance have symptoms of bronchitis developed after their use.

Physiotherapy.—A total of 119 children (57%) were found to be in need of remedial treatment in the department of physical medicine because of defective costal expansion, which in many cases was combined with dorsal kyphosis, round shoulders, and contracted pectoral muscles. It is easy to obtain the co-operation of the older children in breathing exercises. In children under the age of 6 or 7, however, it is possible to encourage breathing exercises only after they are first made breathless by exertion. If this is done one can assist expansion of the lower ribs and correct the child's habit of using the accessory muscles of respiration.

Psychiatry.—There were referred for psychiatric treatment 14 children whose obvious environmental disadvantages in the home or school surroundings seemed to be contributing to the frequency of asthmatic attacks. This number, of course, does not reflect the much higher proportion of children whose attacks may well have had a psychological trigger, developing as a form of escape or induced by the anxiety of parents or as an expression of a jealousy complex developed towards a younger brother or sister. The psychological pattern of the asthmatic child is often extremely complex. High intelligence may be masked by educational backwardness; basic psychological imbalance, perhaps an element in the genesis of the asthma, is difficult to distinguish from those psychological difficulties which arise from educational handicaps and often a semi-invalid regime, and a special and often not wholly natural parent–child relationship. The complexity of this aspect of asthma in childhood, no less than the importance of asthma as a handicap to education and mental development, is shown clearly by the following psychiatric report on an asthmatic child attending the clinic. This report is in many ways a fairly typical one in the more severe cases of the disease.

Psychologist's Report on a Boy Aged 11 Years and 2 Months.—Stanford–Binet ("L" form, 1937) I.Q. 109, mental age 12 years and 2 months. His basic year is 8, while the scatter reveals a lack of fluency and educational retardedness. This backwardness is not due to a lack of intelligence, since he can perform well on the non-educational items at the 14-year-old level. His mental age ought to be at least 13 years and 2 months but for educational backwardness. Tutoring in the basic subjects is suggested, since his backwardness is obviously due to his absence from school because of asthma. He is of average adjustment, introvertively inclined basically, but has good emotional adjustment. Physical symptoms are most apparent in his personality assessment. He attempts to overcome this organ inferiority by being boyishly aggressive against authority. Some adjustment is necessary here, since it would appear that his aggression is a compensation for his strongly felt dependency.

Results of Treatment

Since no random control series is available for comparison, estimates of the effect of treatment are unsatisfactory. Of 179 children followed up for at least six months, 90 had no attack during the six months prior to the time of collection of these data, and 77 had markedly fewer attacks. Two children showed no improvement, and 10 stopped attending the clinic and were untraced. In the whole series there are 44 children who have been free from attacks for more than a year. The group treated by antihistamines and phenobarbitone together, and the group treated by antihistamines alone, were of course selected, and the results of these methods of treatment are therefore not comparable.

Commentary

The age and the sex incidence in this series of 209 children are comparable to those published by previous authors, and the importance of inheritance emerges from our figures as from previous series. Few of the children's own parents have, however, been asthmatic. It seems to be only the allergic tendency which has a genetic relationship. As early as 1916 Cooke and Van der Veer published figures which showed that 48% of the subjects of asthma and hay-fever gave a positive family history, and they conclude that the tendency to allergy has a Mendelian dominant. Hanhart (1940) supported this contention. It is interesting to speculate how in one allergic subject asthma, in another hay-fever, in another rhinitis, and in a fourth eczema is the presenting feature, while in still other patients several or all of these may occur together or alternately.

I have observed that adults who suffer from severe hay-fever may be affected by asthma, which appears to be consequent upon the congestion produced by the hay-fever in the upper respiratory tract and the consequent respiratory obstruction. In other adults asthma has developed after the onset of infection in an antrum or from a badly deflected nasal septum. When an infected antrum is drained or a septal operation performed the asthma has often been relieved. Chobot, Uvitsky, and Dundy (1951) attach great importance to respiratory infection in children as a cause of asthma. The figures I have quoted support this opinion, but I find it difficult to decide from any available evidence, my own or that of others, whether allergy to infecting bacteria or the obstruction produced by inflammatory oedema is prepotent in this connexion. The relief of asthma often obtained in adults by the correction of a deflected septum persuades me that an obstructive element may be important in children too.

The influence of whooping-cough in the initiation of asthma is difficult to assess from my figures. Nearly one-half of the children gave definite histories of whooping-cough, but in only about one-eighth of them did the asthma coincide with or follow immediately after the attack. There is available to me no control series showing how many children in the general population give a history of whooping-cough. One can hardly deduce more than that whooping-cough may be one of the factors which precipitate the onset of asthma in an allergic child.

The high proportion (51%) who had positive skin reactions shows how important protein sensitization is in precipitating attacks.

Summary

A series of 209 asthmatic children attending an allergy clinic in Hampshire over the years 1947–51 is reviewed.

The pattern of asthma as it occurs in the children of the district is outlined.

Reasons for the establishment of a special clinic for the investigation and management of asthma are enumerated.

The importance of such a clinic in reducing the loss of school time and in anticipating the secondary effects which influence wage-earning and even length of life is argued.

So far as it is subject to statistical assessment, the effect of the clinic is examined.

The work of the allergy clinic, no less than the data on which my paper is based, depends to a high degree on the co-operation I have had from the county medical officer of health, Dr. H. L. Cronk, the medical secretaries and records staff of the Royal Hampshire County Hospital, the consulting paediatrician, those colleagues on whom I have depended for specialist reports and treatment, and the general practitioners who have co-operated with me in the management of patients at home.

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LYMPHANGITIS CARCINOMATOSA

BY

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The lesion of lymphangitis carcinomatosa has been known for over a century. First mentioned by Andral (1829), it was later reported by Virchow (1855), and then by Demme (1858), who described seven instances of a condition characterized by marked dyspnoea and a rapidly fatal issue, necropsy revealing wide dissemination of cancerous nodules in lungs and pleurae. Troisier (1873) gave the first fundamental account of the lesions and introduced the term "carcinomatous lymphangitis."

Generalized cancerous permeation of the pulmonary lymphatics is much rarer than the nodular, solid, or linear metastases more usually found, but it gives rise to a far more striking clinical picture, characterized by severe progressive unrelenting dyspnoea. Though the malignant nature of the condition is often appreciated, the site of the primary growth may not be recognized before death. It is in this group of patients that difficulty in diagnosis arises, rather than in those who develop respiratory symptoms while under observation for known malignant disease. The purpose of this paper is to report two new case histories, to discuss the clinical and pathological problems, and to review the literature.

Case 1

A housewife aged 54 was admitted to the General Infirmary at Leeds on August 4, 1950. She had always been healthy, but during the past two to three months she thought she had been losing a little weight, and in the past few weeks had begun to be short of breath on exertion. Two weeks before admission she had a slight cough and wheezing and her dyspnoea increased. When first seen on August 3 she was unable to give a detailed history owing to extreme dyspnoea, and unfortunately she had left her usual private doctor the day before because of his inability to relieve her distress. Apparently she had had a mild digestive upset at Christmas, 1949, characterized by transient anorexia and vomiting, which was ascribed at the time to dietetic indiscretion. In the past few days there had been infrequent vomiting of fluids.

On admission she was ill, cyanosed, markedly wasted, and in considerable respiratory distress. Apart from slight oedema of the feet, abnormal physical signs were confined to the chest, examination of which revealed bilateral pleural effusions, rales, and scattered rhonchi throughout both lungs.

The radiological appearances are shown in Fig. 1. The blood count was normal, and an electrocardiogram showed only left axis deviation. Aspiration produced an orange-coloured fluid which later became haemorrhagic, containing an excess of lymphocytes but no malignant cells. No organisms were seen and the fluid was sterile.

The normal cardiac findings, the gross dyspnoea, marked weight loss, minimal oedema, and absence of ascites, together with the radiological appearances of the lungs, all pointed to malignant permeation of the lungs from an unknown primary source: the complete failure of all treatment added further confirmation.

The patient was given a high protein diet, prophylactic penicillin, and sedation and oxygen as needed. The effusions required repeated tapping, some 15 pints (8.5 litres) being removed in five weeks, though little improvement followed any of the aspirations. Digitalization had no effect. On August 24 she was seen by Mr. G. H. Wooler, who suggested that, in view of the gastric episode the previous Christmas and the occasional vomiting before admission, the primary growth might be in the stomach. Her general condition gradually worsened, respirations averaging 30 and pulse rate 110; dyspnoea finally became extreme, unrelieved by aspirations and hardly influenced by oxygen. Cyanosis persisted to her death on September 9, five weeks after admission. There was no evidence of right heart failure and she was always afebrile.

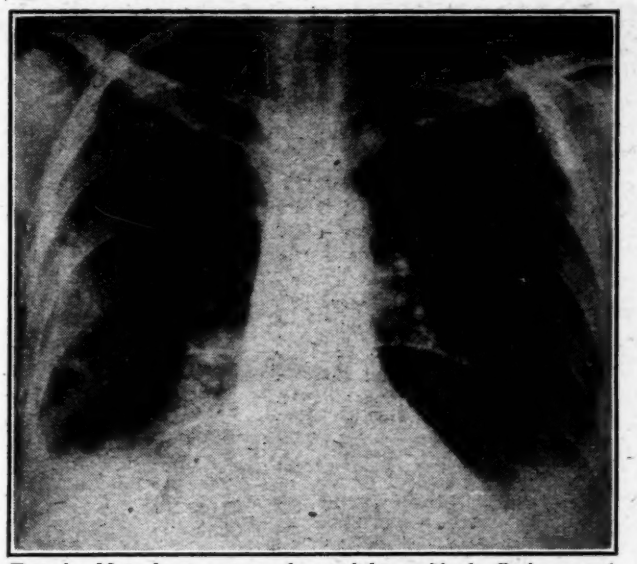

FIG. 1.—Note lower zones obscured by residual effusions, and that mottling, uniformly distributed throughout both lungs, follows a clear-cut reticular pattern. A suggestion of linear striation is seen at the left base, just above the effusion.

Post-mortem Examination

There was a malignant ulcer 3 in. (7.5 cm.) in diameter on the greater curvature of the stomach, immediately above the pylorus, extending across both anterior and posterior walls, with gross thickening of the adjacent mucosa and slight induration in the greater omentum. The pyloric glands on the greater curvature were enlarged and obviously invaded by growth.

The lungs were oedematous, with a peculiar reticular thickening, best appreciated by palpation, characteristic of cancerous permeation of the lung. Both pleural cavities were partly obliterated by dense fibrous adhesions, and each contained a large effusion of clear serous fluid. To the naked eye the hilar glands were normal.

FIG. 2.—Case 1. Lung showing masses of cancer cells in peribronchial lymphatics and partly surrounding a collapsed bronchiole containing mucus.

Histological examination disclosed replacement of the gastric mucosa and muscularis mucosae by a layer of fibrinoid necrosis. Cancerous acini were irregularly scattered through the granulating submucosa, and lymphatic permeation was present in the serous coats, though in the muscle layers only beginning invasion by direct extension of growth was seen. An adjacent gland was largely replaced by growth, which in one part permeated an afferent sinus. The lungs showed diffuse permeation of the perivascular lymphatics by growth, and there were occasional groups of tumour cells within the alveoli (Fig. 2). Where the permeation was heavy there was surrounding fibrosis. Some of the smaller arteries, which were surrounded by cuffs of cancer cells in expanded perivascular lymphatics, were partly occluded by endarteritis obliterans (Fig. 3). On the visceral pleura there was fibrous thickening in relation to the malignant infiltration, and a superficial layer of organizing fibrinous exudate. The hilar glands were not examined microscopically.

FIG. 3.—Case 1. Lung showing a small artery partly occluded by endarteritis obliterans and almost surrounded by a cuff of cancer cells in an expanded perivascular lymphatic channel.

Case 2

A hand sewer aged 34 was seen privately on October 4, 1950. She stated that for four to five years she had had pain in the epigastrium immediately after meals which was relieved by alkalis. For the past two to three months she had been losing weight and appetite and energy, and had noticed a sensation of food sticking in the lower part of her chest, especially solids. In the past few weeks she had become short of breath on exertion, and had been vomiting occasionally in the past few days.

Examination revealed a well-nourished woman with a well-marked aortic diastolic and a short mitral systolic murmur; the heart was otherwise normal, and the blood pressure was 140/90. She was not dyspnoeic at rest. There were no enlarged glands and she was not anaemic. A lump very suggestive of an enlarged spleen could be felt in the left hypochondrium. She was referred to the out-patient department for further investigation, which on October 6 revealed a normal blood picture, negative Wassermann reaction, and an E.S.R. of 15 mm. (Westergren's method); radiological examination of the alimentary tract and chest was arranged.

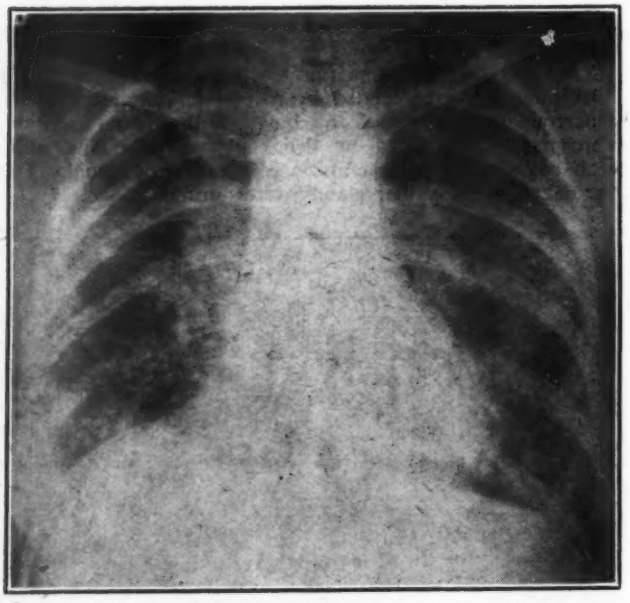

FIG. 4.—Note considerable mottling of coarse reticular type throughout both lungs and small effusion at right base. Opposite anterior end of third right rib are two clear linear streaks. Linear radiation from each hilum is moderately well shown and the hilar shadows are more prominent than usual.

She next attended on November 10, when she was seen by a deputy. She was dyspnoeic at rest, with a persistent non-productive cough, some generalized bronchial spasm, and a small right basal effusion. She said she had spent most of the five weeks since her first attendance in bed owing to her dyspnoea, which had become steadily worse. Radiological examination had been carried out on November 8, and the heart, oesophagus, stomach, and duodenum appeared to be normal; the appearance of the lungs is shown in Fig. 4. A further appointment was arranged, but owing to great increase in breathlessness she had to be admitted as an emergency on November 22.

The clinical picture on admission was dominated by her respiratory embarrassment. Her temperature was 100.2° F. (37.9° C.), pulse 112, and respirations 40. She was cyanosed, but there was no evidence of raised venous pressure or of oedema. In the chest there were widespread rhonchi and medium rales, and a right basal effusion. The cardiac and abdominal findings were unchanged. She was nursed in an oxygen tent, but despite this and treatment with penicillin and antispasmodics her condition rapidly deteriorated, cyanosis becoming more marked and dyspnoea extreme, until she died on November 25.

Post-mortem Examination

The stomach contained a large carcinoma involving the whole posterior wall of the body, and was fixed to the spleen and the tail of the pancreas by adhesions surrounding a mass of enlarged cancerous glands in the greater omentum: 3 in. (7.5 cm.) of the tail of the pancreas was replaced by growth, and the under-surface of the left dome of the diaphragm was studded with cancerous nodules.

The lungs weighed 3½ lb. (1.6 kg.), the right, which showed marked malignant sclerosis of the hilum, being smaller than the left. There was diffuse thickening of the bronchial wall of both lungs and on palpation the parenchyma displayed a firmness which suggested malignant permeation. The right pleural cavity contained a quart (1.1 litres) of serous fluid, and on the visceral pleurae were many diffuse plaques of growth, mainly on the pericardial surface. The hilar glands were invaded by growth. Apart from a bicuspid aortic valve there were no other abnormal findings.

Histological examination revealed a mucoid carcinoma of the stomach composed chiefly of spheroidal cells with some signet-ring forms. The tumour was mainly submucous, but widespread lymphatic permeation in the serous coat had taken place. In the lungs there was widespread peribronchial and perivascular invasion by mucoid carcinoma, especially notable in the pleural and the perivascular subpleural lymphatic channels. Section of a hilar gland showed it to be invaded by widely separated anaplastic tumour cells penetrating the gland capsule.

Radiological Appearances

A full discussion is beyond the scope of this paper, but, in brief, the radiological appearances depend upon a varying combination of (1) linear striation converging radially on the hilum; (2) granular or nodular mottling; (3) reticulation, often very well shown at the periphery; and (4) hilar glandular enlargement. They may be further modified by effusion, atelectasis, or congestive heart failure. The following brief case report illustrates some of the difficulties of diagnosis.

A coal-miner aged 40 was found to have a large carcinoma of the stomach. Radiology of the chest revealed a granular pattern which normally would have been ascribed to his occupation. The presence of a known carcinoma of

the stomach raised the possibility of lymphangitis carcinomatosa, but this was not confirmed at necropsy, when only typical anthracosis was found.

Discussion

By the time of their admission to hospital both these patients were incapacitated by dyspnoea. This was so severe, and its development so rapid, that attention was at once directed to a primary pulmonary cause. Though respiratory symptoms are not infrequently manifestations of malignant disease arising elsewhere than in the lungs, the clinical presentation described above is by no means common. The usual primary sites of growth which give rise to diffuse pulmonary lymphatic permeation are the stomach, bronchus, breast, prostate, and pancreas. Lymphangitis carcinomatosa may precede or obscure or dominate any local symptoms and present as a diagnostic problem in dyspnoea, as in our two patients. It may also occur during the evolution of a growth which has already been identified during life, in which case no clinical problem arises, as in Wu's (1936) 5 personal examples. Wu found in his analysis of 54 examples that a rather younger age group than usual was involved, the stomach being the site of the primary growth in about 75%, the bronchus in some 10%: we believe the proportion of bronchogenic cancer to be rather greater. We feel it useful as well as justifiable to distinguish sharply between these two groups.

Our clinical and radiological findings agree with those of other observers, notably Mendeloff (1945), who pointed out that severe and unremitting dyspnoea is the most common and distressing complaint of these patients. Boccard's (1925) graphic description of "la forme asphyxiante aiguë de la carcinose secondaire du poumon" is well justified. Neither of Mendeloff's two patients had any symptoms or signs referable to the primary site of the tumour. Our second patient had symptoms sufficient to warrant a barium examination of the stomach (with negative results), but no such lead existed in the first. One difficulty in the clinical appraisal of these patients is that general symptoms such as weight loss, weakness, and anorexia, which might in other circumstances be attributed to malignancy, can well be regarded as a secondary effect of the distress induced by severe dyspnoea.

Though the onset of symptoms is often insidious, it may be rapid and dramatic. It may also be precipitated by or occur simultaneously with an upper respiratory infection. In an interesting example reported by Gaines (1935), the initial symptoms of cough and dyspnoea followed and were considered attributable to the inhalation of large quantities of dust. The physical signs are usually slight in proportion to the degree of dyspnoea, mostly consisting of scattered rales and rhonchi, poor respiratory excursion, and sometimes pleural effusion. Asthmatic wheezing is common and was a striking feature of the cases of Mendeloff and of Sweigert *et al.* (1947). Right heart failure may be evident in those patients in whom pulmonary endarteritis has developed with resulting pulmonary hypertension, and Greenspan (1934) published an account of four patients showing carcinomatous endarteritis, two of whom had died with evidence of rapidly progressive right heart failure.

The diagnosis is suggested by the combination of severe dyspnoea out of proportion to the physical signs, a normal heart size, the absence of the usual signs of congestive heart failure, and the characteristic radiological picture. The electrocardiographic findings are of no diagnostic help. Marked loss of weight, if present, is suggestive, and the complete failure of all treatment affords valuable confirmation.

Unfortunately the hilar glands in Case 1 were not examined microscopically: most reports stress their almost constant involvement and a tendency of the growth to prefer lymphatic dissemination. The most satisfactory explanation of the path of dissemination is that of Von Meyenburg (quoted by Jarcho, 1936), which is favoured by most authors. He suggested a retrograde permeation of the pulmonary lymphatics after involvement of the hilar lymph nodes. The preponderance of gastric cancer as the primary tumour is probably an expression not only of the high incidence of cancer in this organ but also of the fact that the lymphatic connexions between its regional lymph nodes and those of the lungs are comparatively short and direct (Wu, 1936). Nevertheless, neither primary blood spread (via the thoracic duct and right heart) nor pleural metastasis with final invasion of the pulmonary lymphatics can be discounted, though both paths seem unnecessarily complicated.

Obliterative changes in the pulmonary arteries are a feature of the histology of Case 1 and of eight of Wu's (1936) patients. The histological changes are mainly of two types—one thrombotic with subsequent organization, the other a true endarteritis. Occasionally the processes are combined. Greenspan (1934) regards these changes as an effect of the perivascular lymphatic permeation; but, while this is widespread, arterial changes may be scanty in relation to it, and some other explanation would seem to be required. Wu believes that the intravascular deposition of carcinoma cells plays an important part in the genesis of the obliterative changes. True endarteritis with intimal proliferation may arise as a result of thrombotic blockage of the lumen elsewhere in the affected vessel, with consequent reduction in the blood flow, or it may be caused by a direct toxic effect of the cancer cells. There is no doubt that generalized cancerous permeation of the pulmonary lymphatics, when associated with obliterative changes in the pulmonary arteries, can simulate the clinical picture of Ayerza's disease, in which dyspnoea and cyanosis are associated with hypertrophy of the right heart. Montgomery (1935), reviewing the literature, stated his opinion that, while the clinical features of Ayerza's disease are clear-cut, the underlying pathological processes may vary widely, and suggested the use of the term "Ayerza's syndrome."

Summary

The case histories of two patients with primary carcinoma of the stomach and generalized carcinomatous permeation of the pulmonary lymphatics are reported. The presenting symptom was severe and progressive dyspnoea, which dominated the clinical picture and overshadowed other evidence of malignant disease.

The clinical and pathological features of the condition are discussed and the literature is briefly reviewed.

We are indebted to Dr. J. G. Benstead for the post-mortem examinations and the histological details, and to Dr. C. Pickard for his assistance in the radiological interpretation.

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According to Lord Milner of Leeds, the name "sanitary inspector" has led to misconception. "The man in the street imagines that a sanitary inspector is a man who spends most of his time examining the drains, occasionally samples the milk, and generally does a number of disagreeable but necessary jobs." Lord Milner was delivering the presidential address at the Sanitary Inspectors' Association's conference at Brighton. He went on to enumerate some of the names which had been tried in the past. Among these were "sanitary police," "sanitarists," "inspectors of nuisances," and "sanitationists." The American version, "sanitarian," had not found much favour in this country (*Manchester Guardian*, September 10).

BLOOD GLUTATHIONE LEVELS AND CARBOHYDRATE TOLERANCE DURING A.C.T.H. THERAPY

BY

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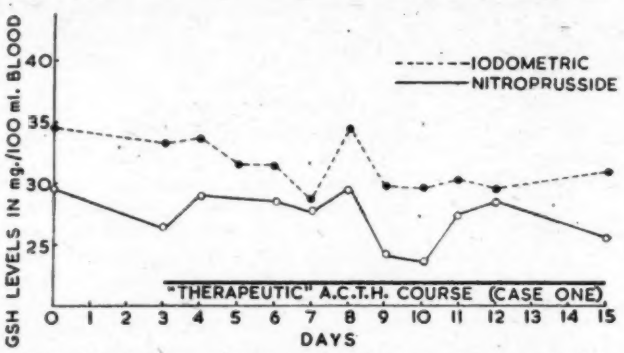
Many biochemical changes in the body following the administration of adrenocorticotrophic hormone (A.C.T.H.) have been described, and these have been studied extensively by numerous workers (see Sprague, 1951). Among them, Conn, Louis, and Wheeler (1948) have reported decreased carbohydrate tolerance, increased uric acid excretion, and a fall in the blood glutathione (GSH) level. They concluded that a metabolic state similar to that in diabetes mellitus had been produced, and that a permanently diabetic condition might result if the administration of A.C.T.H. was continued. Both Conn *et al.* (1948) and Lazarow (1949) speculate on how these changes are produced, and it has been suggested that the fall in the blood GSH level may be due, as in experimental alloxan diabetes, to the presence of some circulating substance which reacts not only with the blood GSH, but also with thiol groups in the β-cells of the pancreas, thereby producing its diabetogenic effects. Attention has also been drawn to the production of experimental diabetes in rabbits by the administration of uric acid (Griffiths, 1948). Conn, Louis, and Johnston (1949) have further claimed that A.C.T.H.-induced hyperglycaemia can be abolished by the administration of GSH. In a study of three patients with rheumatoid arthritis undergoing A.C.T.H. therapy Sprague *et al.* (1950) were unable to confirm the results of Conn *et al.* (1948). While the latter authors' experimental conditions were not exactly fulfilled, no significant changes in GSH levels were noted during treatment.

The GSH levels quoted by Conn *et al.* (1948) in support of their conclusions do not appear to be consistently or markedly abnormal, and it was thought that the relationship between carbohydrate intolerance and GSH levels in the blood during A.C.T.H. administration needed further clarification; this point has also been stressed by Sprague (1951). The levels of blood GSH have therefore been studied in five patients receiving "routine" (I.V.) A.C.T.H. treatment, and in a further group of six patients who were given A.C.T.H. by the same route and in the same dosage as that used by Conn *et al.* (1948).

Methods and Material

Blood glutathione levels have been estimated by two methods: in Cases 1, 3, 4, and 5 duplicate determinations were made both by the iodometric method of Woodward and Fry (1932) and by a modification (Thompson and Watson, 1952) of the nitroprusside method of Brückmann and Wertheimer (1947). The nitroprusside method gives results that consistently are slightly lower than those obtained iodometrically, but as this difference is small, and in view of the close parallelism (see Graph) between the results obtained by the two methods, in the last seven cases blood GSH levels have been measured by the nitroprusside method only. In all cases estimations were made on protein-free filtrates obtained from freshly drawn blood (oxalated or heparinized). Estimations of the packed cell volume were made on all samples.



Relationship between GSH levels obtained by the nitroprusside and iodometric methods.

Observations were made upon 11 patients who had been recommended for A.C.T.H. on therapeutic grounds, and who were seriously ill. Two of them (Cases 6 and 7) had generalized pemphigus of such severity that without A.C.T.H. they would probably have died. Case 9 had moderately severe pemphigus confined to the buccal mucous membrane. Six other patients (Cases 1, 2, 3, 4, 10, and 11) had rheumatoid arthritis, Case 10 being complicated by sarcoidosis and Case 11 by psoriasis. The disease was in all cases severe enough to interfere with their lives, but only Case 11 was bedridden. One severe case of rheumatic fever (Case 8) and one of advanced scleroderma (Case 5) were also included.

Administration

Studies were first made upon five patients who received the following standard course of A.C.T.H. in use in this hospital: on the first and second days, 40 mg. daily, given over eight hours in an intravenous infusion of 540 ml. of 5% glucose-saline; on the third and fourth days, 30 mg. daily, similarly administered; subsequently, 20–25 mg. daily, similarly administered, for about 18 days, with further reductions in dosage in the last days of the course.

By using the intravenous instead of the intramuscular route a great economy in the amount of A.C.T.H. used is made (Duthie, 1952), but difficulties inevitably arise during the course of daily intravenous transfusions, necessitating occasional changes to the intramuscular route, with consequent variations in effective dosage. For this reason, and because of the desirability of reproducing the conditions of Conn *et al.* (1948) as exactly as possible, further studies were made on six patients who each received 50 mg. A.C.T.H. intramuscularly three times daily for eight days, and then small and rapidly decreasing dosages, at first intravenously and then intramuscularly, to avoid the dangerous "rebound" phenomena which have occasionally been observed to follow abrupt cessation of high dosage (Duthie, 1952). In the latter group early morning urine specimens were tested daily for sugar during the course and for a short time before and after it. A glucose-tolerance test was made before starting A.C.T.H. and again on the sixth day of treatment, this day being chosen as Conn *et al.* (1948) found the lowest GSH levels on the fourth, fifth, and sixth days of treatment. The results of these observations are presented in Table I.

Blood GSH levels were estimated on most days, except over the week-ends and for short periods before and after the course of A.C.T.H. These results are presented in Table II. It should be noted that GSH values recorded on day 0 in this Table were obtained before the administration of A.C.T.H.

Results

Response to treatment was judged so far as was possible by objective criteria. In the cases of pemphigus, disappearance of the skin lesions and their failure to recur during treatment was convincing proof of effect. The rheumatoid syndromes and the case of scleroderma were assessed by increase in the range of movement of affected joints.

TABLE I.—*Levels of Blood Sugar Obtained During Glucose-tolerance Tests (a) Before and (b) on the Sixth Day of A.C.T.H. Therapy, and the Appearance of Glycosuria in Fasting Specimens and During these Tests*

Case	Blood Sugar (mg./100 ml.)						Glycosuria	
	0	30 min.	60 min.	90 min.	120 min.	150 min.	Fasting	During G.T.T.
6 a	57	101	135	120	114	—	Nil	—
6 b	111	123	193	232	212	148		
7 a	74	105	—	163	128	185	,,	—
7 b	50	69	150	200	180	180		
8 a	79	93	155	130	118	96	,,	Nil
8 b	92	174	208	142	100	108	,,	Present
9 a	60	85	109	115	97	55	Present	,,
9 b	82	135	124	105	87	75	,,	,,
10 a	78	128	—	111	105	75	Nil	Nil
10 b	98	123	137	114	95	—	,,	,,
11 a	82	122	122	102	97	94	,,	,,
11 b	100	187	234	—	196	76	,,	Present

Improvement in the case of rheumatic fever was shown by the disappearance of symptoms, settling of the fever and pulse rate, and fall in the E.S.R. from about 60 mm. to about 10 mm. in one hour (Westergren). In passing, it was noted that the degree of so-called "A.C.T.H. euphoria" roughly paralleled these objective criteria. In view of the criticisms levelled against eosinophil counts (Rud, 1947) they are not here recorded.

As six good and three fair clinical responses were seen, and the two poor results were both in unpromising subjects, there seems to be no reason to doubt the potency of the A.C.T.H. that was used.

TABLE II.—*Glutathione Levels Obtained Before, During, and After A.C.T.H. Therapy. For Details of Administration and Dosage see Text. Each Course began on Day 0, and the Day of Ending is Indicated by a Bracket*

No.	Diagnosis	Sev-erity	Levels of Glutathione (mg./100 ml. Blood)																	Res-ponse
1	Rh. arthritis	Int.	29·5	—	—	26·2	29·0	28·8	28·5	27·6	—	—	29·5	24·0	28·5	27·4	28·5	26·5	—]	—	—	Fair
2	,, ,,	,,	34·0	35·8	35·0	37·7	36·5	37·0	—	—	42·2	—	42·0	38·0	37·5	—	—	35·5	38·8]	36·0	—	Good
3	,, ,,	Adv.	35·2	—	—	32·0	33·4	36·6	34·8	31·8	—	—	33·0	29·5	28·4	34·6]	—	—	—	—	—	Fair
4	,, ,,	Int.	—	—	29·0	31·4	32·1	36·6	—	—	26·4	27·2	29·1	31·0	32·8	—	—	32·0	34·2]	33·2	36·5	Good
5	Scleroderma	Adv.	—	—	—	31·2	—	—	38·2	—	—	31·0	—	29·8	—	29·0	—	—	29·5]	—	32·5	Poor
6	Pemphigus	,,	—	29·8	26·5	27·6	—	—	25·4	27·5	29·8	27·0	31·0]	—	—	29·5	—	—	—	—	—	Good
7	,,	,,	21·8	—	21·4	—	20·0	—	19·2	—	20·7	20·0	23·5]	—	—	24 0	—	—	—	—	—	,,
8	Rh. fever	Sev.	29·5	31·0	27·8	—	—	30·6	27·7	—	26·1	28·3	—]	—	—	25·5	24·5	25·4	26·6	—	—	,,
9	Pemphigus	Mod.	—	33·0	30·0	35·0	34·8	—	—	31·5	30·2	31·6	34·5]	33·9	—	—	—	31·5	30·0	—	—	,,
10	Sarcoidosis	Adv.	—	44·0	41·6	46·0	41·5	—	—	44·0	41·2	47·0	43·0]	41·2	—	—	42·2	44·0	—	—	—	Fair
11	Psoriasis arth-ropathica	,,	—	31·8	32·6	—	—	32·0	28·8	30·4	36·5	28·0	—]	—	28·5	27·8	32·6	—	—	—	—	Poor
	Day No.	..	−3	−2	−1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	

Studies of carbohydrate tolerance were made in the last six cases, each of which received 150 mg. A.C.T.H. intramuscularly daily. From Table I it will be seen that Cases 6, 7, 8, and 11 showed some degree of carbohydrate intolerance during treatment. In Cases 6, 8, and 11 the values suggested a "lag" type of curve, but in Case 7 results more typical of true diabetes were seen. In Cases 6 and 7 the very extensive skin lesions made the collection of urine samples during glucose-tolerance tests impossible, but glycosuria was seen in Cases 8 and 11 during the second glucose-tolerance test. Case 9 was found to have a low renal threshold before A.C.T.H. was given. In no other case was glycosuria found in the fasting specimens, and these results therefore give no support to Kass, Ingbar, and Finland (1950), who have suggested that the renal threshold for sugar is lowered by A.C.T.H.

The results in Table II were obtained from frequent estimations of blood GSH levels by the nitroprusside method. It will be seen that there is no significant variation in these levels before, during, or after A.C.T.H. administration, although good therapeutic effects were observed.

Discussion

From the above results it is clear that carbohydrate intolerance can be induced by the administration of A.C.T.H., as was observed by Conn *et al.* (1948). In the present series, however, it was never of such severity as to cause the fasting glycosuria that was noted by them, and three of our four cases who showed such intolerance had a "lag" type of blood-sugar curve. It is evident that the degree of carbohydrate intolerance induced in these cases was not so great as that seen by Conn *et al.* (1948). From the therapeutic results there is no reason to doubt the potency of the A.C.T.H., although the possibility must remain that the material used in this work was less active than that employed by Conn. Further, all the present patients were seriously ill, as also were those studied by Sprague *et al.* (1950), whereas Conn's were healthy subjects.

In none of these cases, nor in five others, was the level of blood GSH significantly reduced during A.C.T.H. administration, and no relationship between blood GSH levels and carbohydrate intolerance could be established. This latter finding does not support Conn's hypothesis.

It is quite clear, however, that some degree of carbohydrate intolerance is induced by the administration of A.C.T.H. in some cases by some means. At least one patient has developed permanent diabetes following a course of A.C.T.H. (Glyn, 1951), and persistent hyperglycaemia and glycosuria have been induced in rats by its administration (Ingle, Li, and Evans, 1946).

It does not seem, therefore, that the decreased carbohydrate tolerance induced by A.C.T.H. is regularly accompanied by a detectable fall in the blood GSH level; these results do not support the view that an alloxan-like action initiates the development of transient diabetic states.

I wish to express my thanks for advice and encouragement to Professor R. H. S. Thompson, at whose suggestion this work was undertaken, and in whose department the estimations of blood glutathione levels were made. I am also grateful to Mr. G. Clough and to Miss M. de Jong for their technical assistance. Sufficient A.C.T.H. to treat the last six cases was made available through the courtesy of the Medical Research Council, to whom I am most grateful.

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STREPTOMYCIN FOR CHRONIC AMBULANT TUBERCULOUS PATIENTS

BY

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The use of streptomycin for the treatment of pulmonary tuberculosis has been so intensively studied that it is surprising how little consideration has been given to the largest group of all tuberculous patients—those whose disease is chronic but not incapacitating—who have survived the acute stage of the disease and its accompaniment of treatment, but who will still carry a permanent disability. The early trials, it is true, concerned those whose disease was so advanced that no active treatment was possible, thereby giving moral justification to experiment: later work has been almost exclusively concerned with the clear indications for chemotherapy, such as acute and early exudative disease, tracheo-bronchial disease, and in association with thoracic surgery.

The chronic case has been almost ignored, either because the results are not dramatic enough to arrest attention or because the real nature of the problem has not been properly appreciated. With almost casual indifference most writers and lecturers dismiss the chronic type of disease as beyond the aid of streptomycin. This attitude is probably due to the exaggerated importance given to the *x*-ray appearances, and the fact that so many chronic cases do have extensive cavitation, the course of which is used as the measure of improvement. Streptomycin, of course, cannot of itself close cavities, except in certain cases by its effect upon active bronchial disease. In the type of patient who is now under consideration, however, the radiological appearances are, in any case, unlikely to change very much even as the years pass by, and some other criteria should be used to assess the value of treatment: here, indeed, more than in any other group, is it true that treatment must be directed at the patient and not at his *x*-ray film.

Streptomycin differs from other therapeutic measures in its direct attack on the tubercle bacillus, and in certain types of chronic tuberculosis a bacteriological standard is much more valuable than a radiological one: sputum conversion should be a major aim of treatment. This fact is clearly stated by Tucker (1949): "There can be little quarrel with the validity of sputum conversion as an index of therapy of which streptomycin may be a part."

An investigation has therefore been done to determine the value of streptomycin for this purpose in patients whose only clinical sign of activity has been the persistently positive sputum. The cases have been deliberately selected because they seemed likely to benefit by the treatment, and Fig. 1, which depicts the results of the trial, also indicates the various periods of observation which have been possible. All patients had been under observation for at least six months, and many for more than two years, before starting streptomycin.

The results have been so successful that they have opened up a large field of valuable therapy, and if the continued follow-up confirms the early impressions a most important step will have been taken in the control of tuberculosis.

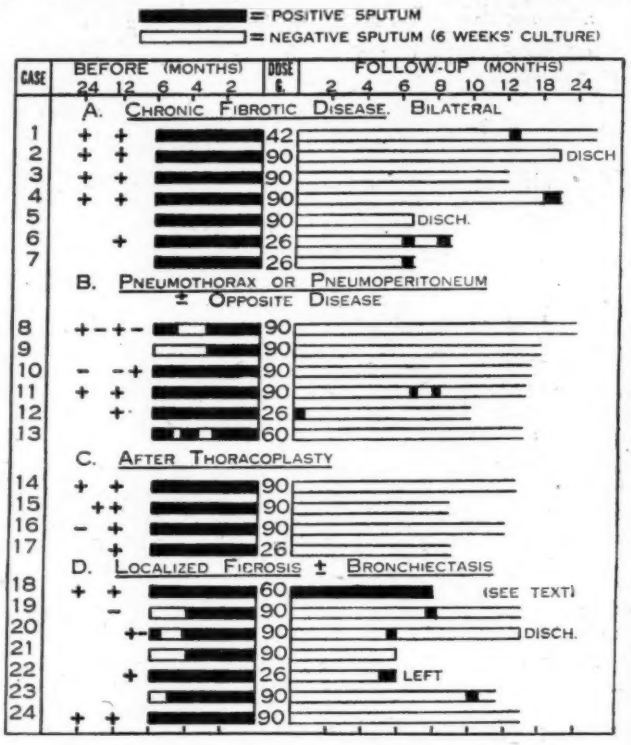

FIG. 1.—Sputum state before and after streptomycin.

Selection of Cases

The investigation was started in February, 1950, and the patients chosen were those whose sputum was persistently positive on fluorescent microscopy or culture but who showed no other signs of clinical activity. They were all men or women working in the Papworth Industries under medical supervision, and living a comparatively normal life. Radiologically there had been little if any change for many months or years; they were regularly afebrile, the blood sedimentation rates were normal, their weight was steady, and the quantity of sputum varied from a trace in the early morning to 2 oz. (57 ml.) daily. No change was made in their normal routine during this treatment.

The following types were included: (1) Patients with widespread chronic fibrotic disease without evidence of gross cavitation, and certainly unsuitable for surgery. (2) Patients in whom a pneumothorax had been established for some months, and in whom the sputum, previously negative, had suddenly become consistently positive. In these cases tomography was done to exclude persistent cavitation. (3) Patients in whom thoracoplasty had failed to convert the sputum, or in whom the sputum had subsequently reverted to positive. (4) Patients in whom the disease had apparently healed by fibrosis and contraction, leaving a slight bronchiectatic condition, but who were unsuitable, or unwilling, for major surgery: it is usually the upper lobes which are thus affected. (5) One patient (Case 18) has been included as an interesting contrast though he did not really fit into this category. He had bilateral apical disease, with fibrosis and contraction, but tomography showed cavitation, 1 in. (2.5 cm.) in diameter, on one side. He refused surgery, and as his general condition was otherwise excellent he was given a course of ambulant chemotherapy, but the sputum was not converted. (Fortunately his views have now been converted instead.)

Sputum Tests

The following standards were observed:

1. Three consecutive positive sputa were obtained before beginning chemotherapy. In those patients in whom a positive sputum was noted for the first time, or there was

a reversion after a period of negative sputa, three more samples taken during a period of about one month were tested to confirm the finding.

2. In most cases samples were tested at monthly intervals during chemotherapy, fortnightly for two months afterwards, and subsequently monthly up to the time of writing.

3. Only 24-hour samples were used; if sputum was not available three laryngeal swabs were used instead of one 24-hour specimen.

4. Sputum was examined by fluorescent microscopy (Cruickshank, 1947) and culture on Löwenstein's medium: a negative report refers to six weeks' culture.

5. The sputum of every patient was tested for streptomycin sensitivity before treatment and found sensitive to 1 unit of streptomycin per ml.

Plan of Treatment

Before starting treatment tomography was done, when necessary, to exclude gross cavitation: in many cases bronchoscopy was also performed and the reports were uniformly normal, thereby excluding tuberculous disease of the larger bronchi as the cause of the positive sputum, since this would demand more drastic treatment. The bronchial aspirate, however, gave further confirmation of the presence of tubercle bacilli.

The course of treatment at first was 1 g. of streptomycin daily intramuscularly, usually for 90 days. P.A.S., 14.1 g. daily, in tablet and cachet form, was given concurrently according to the technique described by Battersby *et al.* (1950). The streptomycin dose has now been reduced to 1 g. twice weekly, for 26 doses, as suggested by recent reports (Veterans Administration, 1951).

Results

The clinical details of these patients are shown in Fig. 1, in which the contrast in the sputum status before and after streptomycin is depicted graphically. The patients are considered in four groups.

A. *Chronic Bilateral Disease.*—Seven men, aged 19–42, had chronic bilateral fibrotic disease which was too extensive for major surgery. Earlier treatment had included medical collapse measures, but in every case the sputum had remained consistently tubercle-positive whilst the patients were under observation at Papworth, which was 6–24 months. There was no gross cavitation. Three of the patients have remained sputum negative. Case 1, the first of the series, was given only 42 g. of streptomycin, and the sputum remained converted for a year. He was then positive to three successive tests, and a further short course of streptomycin was given, which has effectively controlled the disease so far. It is of interest that the two patients given 1 g. twice weekly remained tuberculosis-negative for only about six months, but the chemotherapy will be repeated.

B. *Pneumothorax or Pneumoperitoneum.*—Six cases had an established collapse measure, but the sputum was consistently or intermitttently positive: in Cases 8, 10, 11, and 13 there was also slight disease in the opposite lung. All except one of these patients converted the sputum permanently, and remained tuberculosis-negative up to the time of writing. One man who had been tuberculosis-positive for the previous two years did produce intermittent positive sputum after seven months, but has again been negative for six months.

C. *After Thoracoplasty.*—Four cases were chosen in whom thoracoplasty had been done and in whom the sputum had subsequently been positive for at least a year. All have remained negative since chemotherapy.

D. *Localized Fibrotic Lesion.*—Seven cases had localized unilateral or bilateral fibrotic disease; of these, one (Case 18) also had definite cavitation, and was included because he refused surgery (see above). Of the other six, three have produced one positive sputum since chemotherapy but subsequent tests have been negative, and one has been consistently negative despite being positive for two years previously. Case 22 was given only 1 g. twice weekly, and, although converted at first, he produced positive sputum after five months: unfortunately he left Papworth and has been lost sight of.

Summary of Results

Group:	A	B	C	D	Total
No. in group	7	6	4	7	24
Initial conversion	7	6	4	6	23
Follow-up:					
All tests negative	3	5	4	2	14
Isolated positive	1	1	0	3	5
Reverted „	3	0	0	1	4

The Table shows that of 24 cases with a previously persistent positive sputum, 14 have been entirely sputum-negative since treatment. In five cases an isolated specimen has been positive but subsequent samples negative, and in four cases the sputum which had been converted has subsequently become again positive: three of these received intermittent streptomycin treatment, to a total of only 26 g.

Similar Group (Untreated) for Comparison

The problem of comparable controls in tuberculosis is always difficult and no attempt has been made at alternate selection for this purpose. However, it seemed desirable to compare these results with those of patients in other hostels or under another physician who were living under similar conditions and also working in the Papworth Industries. All such patients who seemed to fall into the same four groups, and who had persistently positive sputum during 1950, were therefore studied; the sputum state of these people is depicted in Fig. 2, the period of observation available being at least a year: no patients with artificial pneumothorax and positive sputum were available, as other forms of active treatment had been initiated.

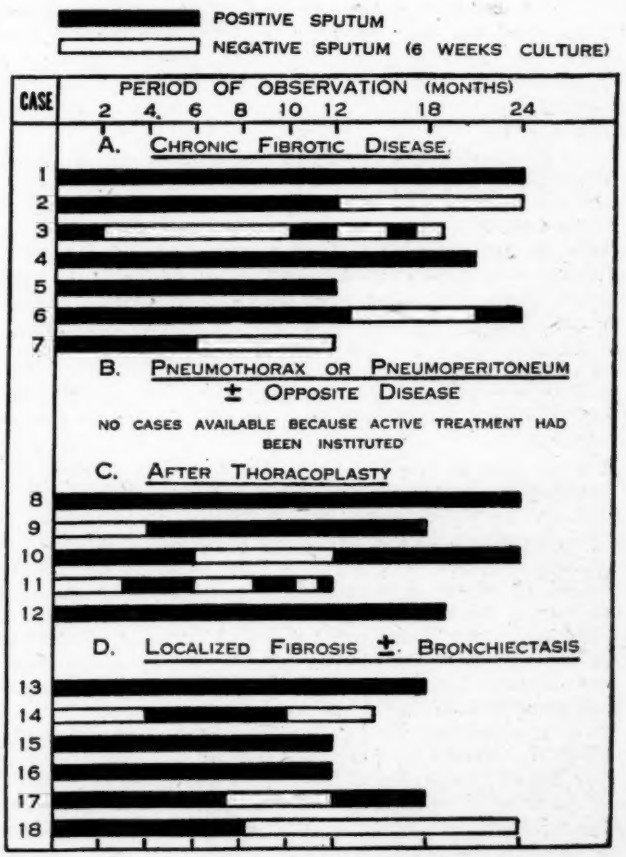

FIG. 2.—Sputum state of untreated group.

On comparison of Figs. 1 and 2 it is immediately obvious that, although certain cases do revert spontaneously—as is well known—there is no clear-cut change such as is seen after streptomycin in Fig. 1.

In addition, of course, the sputum history of most of the patients in the trial series had been recorded during the previous six months to two years, as shown in the left-hand side of Fig. 1, and this record also affords comparison with the post-streptomycin condition.

Complications

Three types of complication might be expected : (1) toxic symptoms due to streptomycin or P.A.S.; (2) development of a resistant strain of tubercle bacillus ; and (3) clinical deterioration.

1. *Toxic Symptoms.*—Since these men and women were continuing at work and living a normal active life during treatment, it was feared that such symptoms as giddiness, visual or aural disturbances, nausea, or diarrhoea would seriously incapacitate them or even be dangerous to those moving among traffic and heavy machinery. No such symptoms have developed in the 24 cases treated, and even the usual abdominal symptoms due to P.A.S. have been much less than is found in bed-patients. In only one case has the diarrhoea due to P.A.S. necessitated a short period off work, and this was ultimately controlled by kaolin. The patients themselves have volunteered the opinion that P.A.S. is much more easily tolerated when they are up and about than when in bed.

2. *Resistant Strains.*—In a community such as Papworth Village Settlement the development of resistant strains of *Mycobacterium tuberculosis* would of course become a serious threat to the families, and before the routine use of P.A.S. this danger would have been very real. In no case in this series has an organism developed resistance to 1 unit of streptomycin per ml. This is in accord with the general opinion to-day that the combination of streptomycin with P.A.S. reduces the incidence of resistant strains from about 70% to 8% (Dunner *et al.*, 1949), or may completely prevent such a complication (Tempel *et al.*, 1950 ; Hughes *et al.*, 1951). The development of resistance to P.A.S. (Carstensen and Andersen, 1950) need not be regarded as a serious problem when compared with the tremendous value of sputum conversion.

3. *Clinical Deterioration.*—The cases were selected carefully, and in no instance has there been clinical deterioration. It is agreed that if patients who really require rest, collapse therapy, or major surgery are treated by ambulant chemotherapy, then the clinician will be practising bad medicine and cannot expect good results. Similarly, extensive cavitation has often been shown to be unsuitable for streptomycin (Tempel and Dye, 1949 ; Riggins and Hinshaw, 1949), although in such patients chemotherapy may be helpful in preventing deterioration whilst awaiting surgery. The usual criteria of weight, well-being, E.S.R., temperature, and *x*-ray appearances were noted throughout the period of follow-up, and in general there was little change. This only indicates the type of disease studied, in which the positive sputum was the main adverse clinical finding.

Discussion

Topical interest is focused on the falling death rate for pulmonary tuberculosis, but this fact combined with intensified survey work may well aggravate the immediate public health problem. The chronic patient who is kept alive in 1952 must be controlled, and if possible employed, and even the most enthusiastic physician will hardly claim that all such patients can be really cured and rendered non-infectious. Heaf (1951) mentions a figure of 140.000 persons "at large in England and Wales . . . and potential sources of infection," and of these a large proportion will be of the type referred to by Gloyne (1946) as "indolent tuberculosis."

In America the expression "grumblers" is used (Howlett and O'Connor, 1948), a term which describes both the clinical condition and often, alas, the mental state which is engendered by the lack of treatment or employment and by the surfeit of commonplace advice.

If we feel it our duty to prolong life, it must also be our duty to do everything in our power to enable these persons to obtain such employment as is within their powers. Longevity without peace of mind or economic independence is a sad prospect.

The problem of the "good chronic" is the most tragic and difficult in tuberculosis work, and the patients chosen for this series represent those who do attend at every clinic and promote anxious discussion among chest physicians. Such patients are often able and willing to work, being in fact compelled by economic pressure to do so. Yet employers and physicians take fright at the thought of possible infection. At a recent interview, 10 out of 14 men wishing to come to Papworth had been prevented by their tuberculosis officer from obtaining local employment because the sputum was positive, and this enforced and unnecessary idleness had lasted from one to three and a half years. One should think not only of the personal tragedy involved but the economic cost of unemployment, and the frustration and incompleteness of medical care.

Neither medical nor surgical treatment is yet completely curative, and thoracoplasty often leaves a persistent positive sputum although the disease appears inactive (Holmes Sellors, 1947 ; Thompson, 1951 ; M.R.C., 1951). Gutheil *et al.* (1950) reported 20% of cases with a positive sputum 10 years after thoracoplasty, and successfully used streptomycin for sputum conversion. These are the men and women who should be helped back to employment and more certain cure.

The significance of a positive sputum will not be discussed fully, but reference can be made to Berg (1939), Chang (1948), Abeles (1948), and Brieger (personal communication), who have shown that the survival rate is considerably lower in patients with a positive sputum, and the incidence of relapse is higher. This applies even to the patient with intermittently positive sputum after apparently adequate treatment. The importance of the public health problem, of course, needs no emphasis, and the dictum of Tucker (see above) will be generally approved.

The results of this series have shown that in selected types of cases the social and medical disadvantage of an infectious sputum can be prevented without interfering with the usual routine of life. The patients continued their active work and social life during treatment, remaining economically independent and able to support their families without assistance.

The same possibility exists for physicians working from chest clinics, and there is no reason why such treatment should not be given either in the out-patient department or by visits from the clinic nursing staff : there would be no need for a man to give up his employment. If further study confirms the results of Tempel and Dye (1949) and of most speakers at the tenth Streptomycin Conference (Veterans Administration, 1951) that intermittent dosage is equally effective, the arrangements for treatment at a clinic would require only simple organization.

The cost of such treatment would be negligible compared with the cost of financing unnecessary idleness, even though different sections of the Exchequer were concerned.

Warning must be given, of course, that it is essential for such treatment to be under the direction of a chest physician with adequate facilities for bacteriological control.

Conclusion

The physician to-day should not be satisfied with merely rendering his patient quiescent and jogging him along "under careful observation," State-supported, and only half enjoying life. The goal should be a man whose disease is inactive, who is financially independent, and who is no risk

to his family or colleagues. With this in view, there is considerable scope for chemotherapy in certain types of more chronic patients whose only real disability is an infectious sputum, and this series of cases has shown that the sputum can be converted without interfering with the ordinary day's work.

Summary

Streptomycin and P.A.S. have been used for certain types of patient whose only adverse clinical sign was a positive sputum. Twenty-four patients, in four categories, whose sputum was consistently positive, were treated without interfering with their work or ordinary life.

In 23 cases the sputum was converted; in 14 of them it has remained negative up to two years. Five patients have since had an isolated positive sputum, and four have reverted to positive sputa after being sputum-negative for a period.

The value of such results is discussed when applied to the problem of employable chronic patients, so commonly attending chest clinics.

I am grateful to Dr. R. R. Trail and Dr. L. B. Stott for their advice in the presentation of this paper, and to Dr. K. M. A. Perry, Dr. D. Barron Cruickshank, and Dr. R. B. Murphy for assistance in the selection and treatment of the cases.

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The possibility of using high-velocity electrons and gamma rays for sterilizing pharmaceutical products was discussed by Government scientists and representatives of the pharmaceutical industry at a recent meeting at the Department for Scientific and Industrial Research. The method, according to Dr. R. S. Hannan, who has been studying the problem in America, has several advantages: it permits the sterilization of heat-sensitive materials; almost any type of sealed container can be used for the process; and it may lead to the preparation of new products, such as new vaccines. One of the disadvantages is the high capital cost of the generating equipment. Electron accelerators at present available in Britain, capable of treating 1 cwt. (51 kg.) of product an hour, cost between £25,000 and £50,000. A cobalt 60 source for producing gamma rays in sufficient quantity to sterilize 7 lb. (3 kg.) a day would cost £2,000, but gamma rays from fission products would be much cheaper. Other disadvantages, perhaps more theoretical than practical, are toxicity from unusual chemical by-products of irradiation and the failure to inactivate enzymes. The energies used for sterilization are insufficient to induce radioactivity in treated products. So far most of the work in this country on "electronic sterilization" has been done in relation to food; however, its uses in this field may be limited because of alterations to flavour.

ACQUIRED HYPERSENSITIVITY TO SODIUM P.A.S., STREPTOMYCIN, AND PENICILLIN

BY

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The administration of sodium *p*-aminosalicylate together with streptomycin is at present the most effective form of chemotherapy for tuberculosis. Toxic effects, while not infrequent, are usually of minor degree. Occasionally streptomycin produces a more severe reaction, such as exfoliative dermatitis or agranulocytosis, which may endanger life. The liver, however, generally appears to escape damage and jaundice is not a feature.

It was at first thought that the toxic effects of P.A.S. were mostly confined to the alimentary tract, the characteristic symptoms being nausea, vomiting, and looseness of the bowels; these disappeared rapidly on stopping the drug. Recently, however, it has become apparent that a small proportion of patients can develop an acute hypersensitivity with severe systemic upset, and a number of reports (Cuthbert, 1950; Livingstone and Street, 1950; Hess and Ismay; 1950) have indicated that P.A.S., in the form administered, is potentially hepato-toxic.

The case here reported is of a patient who developed a most profound systemic reaction following the administration of sodium P.A.S. and streptomycin, with exfoliative dermatitis, liver and kidney damage, and an intense bone-marrow response. Later she had a reaction to penicillin.

Case Record

A single woman aged 23 was admitted to hospital on January 25, 1950, with a cavity at the right apex; sputum positive. Thoracoplasty was recommended, but before it could be carried out the disease spread to the right mid-zone. To control this streptomycin (1 g. daily) and sodium P.A.S. (18 g. daily in divided doses) was begun on March 24.

Stage 1 (April 13–19): *Prodromal Symptoms.*—On April 13 the temperature rose suddenly to 100° F. (37.8° C.) and slight headache ensued. Both drugs were continued, as other patients had had similar reactions, which settled in a day or two. Temperature fell to 99° F. (37.2° C.) and patient felt better. On April 19 the leucocytes numbered 6,100 (eosinophils 10%).

Stage 2 (April 20–28): *Exfoliative Dermatitis.*—On April 20, after 27.5 g. streptomycin and 504 g. P.A.S., patient complained of nausea, dyspnoea, and pain in right side of chest. Temperature rose to 101.4° F. (38.6° C.). Next day she had a rigor and vomited; temperature 103.4° F. (39.7° C.). An intensely irritating maculo-papular rash appeared on the abdomen and rapidly became generalized, affecting particularly extensor surfaces of the forearms and legs, where it soon became vesicular and later haemorrhagic. Face swollen and puffy; glands in posterior triangle enlarged and tender. Tongue and inside of mouth became ulcerated; swallowing, even of fluids, was exceedingly difficult and painful. Motions were loose (no pathogens isolated); urinary output fell to 15 oz. (425 ml.) a day. Leucocytes numbered 44,000 (eosinophils 19%) on April 25, and 70,000 (eosinophils 19%) on

April 27. This high count was probably due in part to haemoconcentration, as erythrocytes rose at the same time by a million cells per c.mm.

Stage 3 (April 29–May 11): *Liver and Kidney Damage.*—On April 29 temperature again rose suddenly to 103.6° F. (39.8° C.), and remained elevated for three more days. Urine (May 1) contained albumin and numerous granular and leucocyte casts; on May 3 sclerae were yellow and the liver edge, though barely palpable, was tender. Urine (May 4) showed large excess of urobilin and urobilinogen, but no bile salts. Thymol turbidity (May 5), 20 units; serum alkaline phosphatase, 49 units. Van den Bergh reaction, direct positive. Stool pale in colour. Temperature rose to 103.8° F. (39.9° C.) on May 7, with subsequent deepening of the jaundice. E.S.R. (3/12 on April 21) rose to 78/104 on May 6. Patient showed signs of mental confusion, and complained of tingling in hands and feet. Right plantar response definitely extensor, left doubtful. Blood urea (31 mg. on May 5) rose to 99 mg. on May 9. On May 10 urine still contained albumin and casts, but leucocytes had fallen to 8,900 (eosinophils 14%).

Stage 4 (May 11 onwards): *Recovery.*—Temperature returned to normal. Skin began to peel extensively all over the body. Tongue improved greatly and patient was able to swallow normally. Jaundice faded and the liver lost its tenderness. Thymol turbidity test gradually fell to normal. Urine returned to normal. Hair on scalp fell out as the skin peeled, but later grew strongly. Skin remained roughened and itchy for several weeks.

During the whole period of the reaction there was no extension of lesions in the lungs, and a radiograph taken with a portable machine (April 21), with rash at its height, actually showed improvement, the previously noted spread in the right mid-zone having cleared. A film (May 12) after the period of jaundice and albuminuria showed no extension of disease, but a later film (June 9) revealed a new wedge-shaped area of consolidation in the right upper zone with a central cavity. Sputum increased from a trace (positive) to 5 oz. (130 ml.) (also positive), and cough became troublesome. Later this area slowly resolved and two-stage thoracoplasty was performed (December 6 and 21).

Post-operatively, an acute effusion developed within two days in the Semb space, and on January 9, 1951, aspirated fluid grew *Staph. aureus.* Penicillin, 1,000.000 units twice daily, was administered, but had to be stopped when widespread punctate rash developed on trunk, face, and limbs. The patient then made an uneventful recovery and was discharged from hospital well and sputum-negative on April 20.

Treatment

Streptomycin and P.A.S. were discontinued on April 20, when the generalized rash appeared. Diphenhydramine hydrochloride, 50 mg. twice daily, was given by mouth, and mepyramine hydrogen maleate cream applied to skin. Later, mepyramine, 100 mg. thrice daily, and promethazine hydrochloride, 25 mg. at night, were tried, but produced little significant change. Twice-daily intravenous injections of calcium gluconate (10 ml.) brought about temporary alleviation of the intense itching, but were otherwise unhelpful. Intravenous sodium thiosulphate produced no alleviation. Lotio calaminae with phenol 1% had a soothing effect locally. Following adrenaline, 0.5 ml. subcutaneously every six hours, the rash began to subside and the eosinophil count fell rapidly, but it would be unwise to conclude that the adrenaline was the responsible agent. It is worth noting that sunlight appeared to exacerbate the rash and increase the irritation.

The sore mouth was a distressing feature. Vitamin-B complex was given, and considerable relief was obtained by the patient retaining in her mouth for several minutes at a time a 1:6 solution of sodium sulphate. She was encouraged to take glucose and protein drinks. Potassium citrate, 30 gr. (2 g.), was given six-hourly.

Subsequent Investigations.—A series of patch tests was carried out on the forearms and repeated on the back. There was a strong reaction to sodium P.A.S. 5%, to meta-aminophenol 1%, to streptomycin, and to dihydrostreptomycin. Sodium salicylate up to 20% produced no reaction.

A test dose of 3 g. P.A.S. by mouth resulted in a sharp rise of temperature to 101° F. (38.3° C.) associated with headache and reappearance of a papulo-vesicular rash on the extensor aspects of forearms and legs. A test dose of 0.5 g. streptomycin intramuscularly produced a generalized papular rash which faded within three days; there was no temperature reaction or eosinophilia.

Discussion

Acquired hypersensitivity to P.A.S., streptomycin, and penicillin has been recorded by McKendrick (1951), whose patient, a man aged 27, also developed hepatitis following a rash. As in the present instance, streptomycin and P.A.S. were given together. While it may be difficult to determine which drug was the original precipitating factor, there is evidence that the administration of P.A.S. is apt to result in liver damage. Streptomycin in the pure form now available seems to have little or no deleterious effect on the liver, either in human beings or in the experimental animal (Riggins and Hinshaw, 1949). P.A.S., on the other hand, has several times been said to produce hepatitis when administered alone (Cuthbert, 1950; Scott and McCann, 1950; Livingstone and Street, 1950). The reaction to P.A.S. seems to be violent and tissue damage severe, but a fatal outcome is generally avoided; indeed, complete recovery appears to be the rule, although it is highly probable that the state of hypersensitivity persists indefinitely. Desensitization is practicable, but should not be expected to be effective against drugs other than the one in question, and even then its action may not be permanent.

Sensitivity to streptomycin and penicillin, though not common, is to some extent explained by the fact that there is some slight antigenic similarity in the products of all fungi; thus Bedford (1951) describes a different example of the same thing—a violent reaction to aureomycin in a patient known to be sensitive to penicillin. Even the ordinary tinea infection of the feet and groins appears to possess this common antigenic property. The simultaneous acquisition of sensitivity to P.A.S. and streptomycin, however, seems to occur too often to be explained on the basis of an increased liability to develop multiple sensitizations in a potentially allergic individual. Nevertheless, at present there does not seem to be an alternative explanation. It is our impression, however, that a patient who has become sensitive to P.A.S. is particularly apt to exhibit toxic phenomena when other drugs are administered. Thus, another patient in this hospital who initially became sensitive to P.A.S. has since reacted violently to streptomycin, penicillin, and "sulphatriad" (but not to thiosemicarbazone).

It is also apparent that P.A.S. may cause hypersensitivity to certain chemically allied substances; this fact does not seem to have been stressed in previous reports on the subject. Mayer (1928) first noted that sensitization caused by substances containing an aminophenol group may on occasion be caused by that group and not by the whole molecule. He explained this by showing that the skin transforms all these substances to quinone-imines and di-imines, or their derivatives, and that it is to these that the reaction occurs. Although sensitization may occur in this manner with *any* aminophenol group, it is when the amino radical is in the *para* position that it is commonest. This cross-sensitization is illustrated by two further cases of P.A.S. sensitivity which we have seen. One developed an acute generalized skin rash when given 0.5 g. sulphatriad by mouth, while the other gave markedly positive patch tests to 1% dilutions of P.A.S., *para*-aminobenzoic acid, sulphanilamide, procaine, *para*-phenylenediamine (the active ingredient in a well-known hair dye), *meta*-aminophenol, and *para*-aminophenol. The reaction to *para*-aminophenol was distinctly more pronounced than that to *meta*-aminophenol.

It is our belief that P.A.S. itself can be responsible for producing sensitization and that *meta*-aminophenol, some-

times present as a contaminant in P.A.S., need not be invoked as the guilty agent. Thus the use of freshly prepared solutions only, while desirable, will not necessarily prevent the development of P.A.S. sensitivity. For the patient's future safety we advocate patch testing in every known instance of P.A.S. sensitivity, at least against the drugs mentioned. These substances are commonly used in medicine to-day, and the list of drugs containing an aminophenol group is very long, including, among others, sulphadiazine, sulphaguanidine, and picric acid. Testing against the sulphonamide group of drugs is of special importance because of their wide general application. Procaine *may* be equally important, but we have used it as an anaesthetic agent in several P.A.S.-sensitive patients without apparent ill effect.

With regard to the more specifically tuberculous aspects of streptomycin–P.A.S. sensitivity, the possibility of this development can no longer be ignored when considering the application of chemotherapy in a patient suffering from tuberculosis. Besides the risk of damage to the liver, kidney, skin, and other organs (including possibly the central nervous system) further treatment may be prejudiced—particularly resection, should this be required. P.A.S., because of its alleged harmlessness, has perhaps been employed rather more freely than would otherwise have been the case, but present knowledge of the profound bodily disturbance it may cause emphasizes the need to avoid indiscriminate chemotherapy.

It should be mentioned that our patient had no previous history of allergic phenomena other than a mild upset, possibly due to food, during childhood. The hypersensitivity appeared to develop purely as a result of drug administration. The severity of the reaction which occurred is all the more disturbing because there is no direct clue regarding which patients are likely to prove susceptible. When administration of the drug has begun, however, *particular attention should be paid to any unexpected rise of temperature, especially during the period two to four weeks after the beginning of treatment*, which appears to be the usual time for reactions to develop. In patients who have had P.A.S. previously, hypersensitivity may of course occur much earlier.

Finally, the possibility that P.A.S.-sensitive patients may develop local sensitization phenomena must be remembered. Our patient had a severe effusion into her Semb space following thoracoplasty, and, in retrospect, the possibility of its being due to the sulphathiazole–penicillin powder dusted into the space at operation has to be considered, although no generalized rash developed at the time. It is, on the whole, perhaps advisable to avoid using sulphathiazole powder or tablets in this way in P.A.S.-sensitive patients.

Treatment of the condition with A.C.T.H. was considered, but at the time it was felt that the danger of producing spread of the tuberculous lesion was best avoided. If A.C.T.H. had been administered it would have been difficult to avoid the charge that it was responsible for the spread of disease in the right lung, which did, in fact, occur after the acute reaction had settled down. Even so, the employment of A.C.T.H. in carefully graded doses remains a possibility in patients with tuberculosis who have developed acute drug-sensitivity.

Summary

The case history is given of a patient who suffered from a severe general toxic reaction to combined P.A.S.–streptomycin. Skin, alimentary tract, liver, kidney, and bone marrow all gave evidence of considerable damage, and the central nervous system may also have been affected. The patient later developed hypersensitivity towards penicillin.

Treatment adopted is outlined. Particular attention should be given to the mouth and to the protection of the liver by the administration of glucose in the early stages. The patient's skin should be protected from direct sunlight.

As a preventive measure it is important to stop P.A.S. *as soon as any unexpected rise of temperature occurs*; in susceptible patients this usually occurs two to four weeks after the beginning of treatment.

If sensitivity to P.A.S. has already developed it would seem that reaction to other drugs may more readily occur, particularly those containing an aminophenol group in the *para* position—for example, certain sulphonamides, picric acid, hair dye. The routine patch testing of P.A.S.-sensitive patients towards such drugs is advocated; it is preferable to begin with a 1% solution of each. The patient should be told what drugs to avoid.

The mechanism whereby hypersensitivity to a heterogeneous group of drugs becomes established is not properly understood and requires further elucidation. The mechanism of desensitization would also repay fuller investigation.

The development of drug hypersensitivity imposes limitations as regards future treatment; this aspect further emphasizes the need to avoid indiscriminate chemotherapy.

A description of this case from the nursing point of view, by Sister J. Kenshole, appeared in the *Nursing Mirror* of November 16, 1951, p. 151.

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TECHNIQUE OF JELLY (TUBERCULIN) TESTING

SOME FURTHER OBSERVATIONS

BY

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Recent correspondence in the medical journals shows that all physicians are not yet satisfied with this test. This may be due to technique, for it has been shown (Lendrum, 1951) that the test as described gives better results than the 10 T.U. (tuberculin units) Mantoux test, although fewer positive findings than the 100 T.U. test—perhaps an advantage when the non-specific element of the latter is taken into account (Long and Seibert, 1937; Furcolow *et al.*, 1941; Furcolow and Robinson, 1941; W.H.O., 1948).

When Dick (1950) described the technique, using flourpaper and P.P.D. jelly, he noted a discrepancy in results between P.P.D. and O.T. jellies which he was unable to explain and which I, having noted the same discrepancy independently, suggested was due to insufficient lapse of time before the test was read.

The investigations reported here are considered to be of importance, as they explain the discrepancies in results, as well as the dissatisfaction of some physicians.

Storage at Room Temperature

A number of tests were performed on schoolchildren aged 5 to 17, using (1) O.T. jelly kept in a refrigerator throughout, and (2) O.T. jelly of the same batch (A. & H. 371) stored for from 11 to 15 months at room temperature, results being read on the *fifth* day. The technique of the test is as follows: A firm rub with a plug of cotton-wool soaked in *acetone* is given to the interscapular area to be tested, followed by six *light* strokes with flourpaper. The minimum thickness of jelly is applied to the area in a recognizable shape (the letter T is used, as this gives a right-angle, as opposed to the acute angle of the V usually recommended) and covered with adhesive plaster, firmed as close into the T as possible. The plaster is kept dry and removed at 48 hours.

TABLE I.—*Effect of Storage at Room Temperature, Read on Fifth Day*

		Results by O.T. Jelly Stored in Refrigerator	
		Positive	Negative
Results by O.T. jelly stored at room temperature	Positive	319	Nil
	Negative	4	676

Table I shows that out of 999 individuals whose tests were read on the fifth day only four gave differing results, to the disadvantage of the R.T. jelly.

Serial Results Using O.T. and P.P.D. Jelly

A group of children aged 5 to 17 years were tested by both types of jelly at the same time, by the same described technique, the results being read serially. All who were absent for one reading are excluded. The group whose initial reading was on the fourth day were all aged 11 or more.

TABLE II.—*Serial Readings*

A. *Third to sixth day, all age groups*

Day 3		Day 4		Day 5		Day 6	
O.T.	P.P.D.	O.T.	P.P.D.	O.T.	P.P.D.	O.T.	P.P.D.
+ −	+ −	+ −	+ −	+ −	+ −	+ −	+ −
211 424	180 455	223 412	209 426	230 405	222 413	232 403	227 408
635		635		635		635	

B. *Fourth to seventh day, aged 11 and over*

Day 4		Day 5		Day 6		Day 7	
O.T.	P.P.D.	O.T.	P.P.D.	O.T.	P.P.D.	O.T.	P.P.D.
+ −	+ −	+ −	+ −	+ −	+ −	+ −	+ −
76 73	76 73	84 65	83 66	84 65	83 66	83 66	83 66
149		149		149		149	

Table IIA shows that the number positive on the third day was 211 with O.T. jelly and only 180 with P.P.D. jelly (a similar degree of difference to previous findings); by the fifth day the figures were 230 by O.T. jelly and 222 by P.P.D. The rise in positive results is 19 (3% of the total examined) with O.T. jelly and 42 (6.6%) with P.P.D. jelly. The further rise on the sixth day is slight, and greater for the P.P.D. group.

Table IIB shows little difference between the two groups, but again demonstrates that a rise in positive rates occurs between the fourth and fifth days (51% to 56.4%).

Serial Results with O.T. Jelly

Two groups of children were examined, all aged 5 to 17 years. The group initially read on the third day had a majority under 11 years; the other group had a majority of 11 years and over. Results were read towards the end of the day shown; thus the third day's result was read between 66 and 72 hours after application of the jelly.

TABLE III.—*Serial Readings, Using O.T. Jelly*

A. *Third to sixth days*

Day 3		Day 4		Day 5		Day 6	
+	−	+	−	+	−	+	−
243	503	258	488	269	477	273	473*
746		746		746		746	

B. *Fourth to seventh days*

Day 4		Day 5		Day 6		Day 7	
+	−	+	−	+	−	+	−
249	261	269	241	273	237	261	249†
510		510		510		510	

* Includes 63 negative on the first three days and assumed negative on the sixth day.

† Includes 162 negative on the first three days and assumed negative on the seventh day.

In one school the authorities did not wish those children who had had three negative readings to leave for a fourth time; some of these might have become positive on the fourth reading, and thus have stressed the tendency of the number of positive results to increase with time.

Table IIIA shows that the 243 tests positive to O.T. jelly on the third day had risen to 269 by the fifth day and to 273 by the sixth, or from 32.6% on the third day to 36.1% on the fifth day, a rise of 3.5%.

Table IIIB shows, again, a considerable rise between the fourth and fifth days, from 249 to 269, or from 48.8% of those examined to 52.7%, a rise in this group of 3.9%.

Discussion

Storage of Jelly.—The results in Table I show that no significant loss of potency occurs in O.T. jelly resulting from storage at room temperature. The usefulness of the test material, by the prevention of waste and by making refrigeration facilities unnecessary, is thus confirmed. Its other advantages have been discussed previously.

Effect of Time on Results.—The importance of the time factor was seen during the previously reported work on skin testing, when it was observed that, in a school where 312 boys were tested, 14 showed a change from negative to positive with the passage of time using P.P.D. jelly, and four with O.T. jelly. The serial results in Table II show that there is a *progressive* rise in the number of positive results with both types of jelly from the third to the sixth days; they also show that the increase is greater for P.P.D. jelly than for O.T. jelly. Dick (1950) was unable to give an explanation of the discrepancy in results from the two jellies; as his results were read at 72 hours, the time factor is seen to be the explanation. In the present series, 6.6% of those examined (Table IIA) would have given false negative results with P.P.D. jelly as judged by the findings on the fifth day. These findings and those in Table III also show why some physicians are dissatisfied with results. Most seem to read their results on the third day (Lendrum, 1951), but Table IIIA shows that there is a rise of 3% in positive results with O.T. jelly between the third and fifth days, and a higher percentage in the older age groups. Table IV shows this rise as a percentage of the total examined in each group, serially.

TABLE IV.—*Rise in Percentage of Positive Results with O.T. Jelly*

Source	Between Days			
	3 and 4	4 and 5	5 and 6	6 and 7
Table IIA ..	1·9%	1·1%	0·3%	
,, IIIA ..	2·0%	1·5%	0·5%	
,, IIB ..		5·4%	Nil	Fall
,, IIIB ..		3·9%	0·8%	,,

It is apparent from the serial results that in some cases fading was taking place on the sixth day; and there was a fall on the seventh day in the number which, seen for the first time, could be called positive.

The fifth day would therefore seem to be the optimum for reading O.T. jelly tests. The few who may be missed will not be of significance from the clinical point of view, as those with active disease are likely to become positive before this day. It may be a minor disadvantage in the field to test prior to B.C.G. inoculation, but this must be offset against the disadvantage of the non-specific reaction to the 100 T.U. Mantoux test. A considerable number of false-negative results will be obtained if readings are made only on the third day.

Consistency of Serial Positive Tests with O.T. Jelly.—It is of importance that the increasing number of positive results up to the sixth day should include *all* those previously positive in the serial readings. Among the 746 individuals whose tests were read from the third to sixth days (Table IIIA) there was, in fact, one discrepant result—a negative on the fourth day, the remaining three readings being positive; this is interpreted as a false positive on the third day. One case positive on days three, four, and five was negative on the sixth day. Of the 510 persons tested from the fourth to seventh days (Table IIIB) only one who was positive on the fourth day became negative before the seventh day, although 13 who were previously positive were negative on that day. This one case was positive on the fourth and seventh days and was recorded as negative on the fifth and sixth, and does demonstrate an error in technique—of testing, reading, or recording. In referring to false positive results, Dick's advice that a control be used until one is thoroughly conversant with the method is very sound. It is not only plaster reactions which may cause doubtful results (although these are avoided by reading on the fifth day); I have heard of some physicians who accept the mother's word for the result. With regard to false-negative results, it is important that the same piece of flourpaper shall not be used on more than one individual.

Summary and Conclusions

Simultaneous tests on 999 children using O.T. jelly stored in a refrigerator and at room temperature for a period of from 11 to 15 months show only four differences in results on the fifth day. The jelly may therefore be kept at room temperature without loss of potency.

A series of tests using O.T. jelly and P.P.D. jelly simultaneously and read serially confirms the previously reported findings that O.T. jelly gives a higher proportion of positive results on the third day than does P.P.D. jelly, the differences between the two being 3.6% on the third day, 1.3% on the fifth day, and 0.8% on the sixth day. Thus the previously unsatisfactory results with P.P.D. jelly are seen to be due to the fact that it is later in giving positive reactions.

A series of tests using O.T. jelly only and read serially shows a progressive rise in positive results up to the sixth day; on the sixth day one test previously three times positive became negative and reactions tended to fade. On the seventh day 13 reactions previously positive on three occasions had become negative. The optimum day for the reading of O.T. jelly tests is therefore the fifth day, but this may be extended to early on the sixth day. Tests should not be read as early as the third day, as there may be a significant number of so-called false-positive tests due to plaster reaction and other factors, and as there will be an appreciable proportion of false-negative reactions. The seventh day shows a fall in the number of positive reactions.

Serial readings in a series of 746 individuals show that only once did a positive result become negative before the sixth day; this is regarded as a false-positive result on the third day, which should not be used for reading. In another series of 510 individuals one case was recorded as positive on the fourth and seventh days and negative on the fifth and sixth. This is admitted to be an error of technique, and stresses the need for controls. Thus, in a total of 1,256 individuals, only one case read on the fifth day gave a result possibly inconsistent with the true tuberculin state as shown by other serial readings; these have been shown previously to give results between those found with the 10 T.U. and the 100 T.U. Mantoux test.

I wish to thank Dr. J. Knowelden, of the Department of Medical Statistics, London School of Hygiene, for his advice and assistance.

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Medical Memorandum

Ununited Fractures of the Clavicle

There are few reports of ununited fractures of the clavicle in the literature. The two largest series are those of Berkheiser (1937) (nine cases) and Ghormley *et al.* (1941) (20 cases). These latter were collected from the records of the Mayo Clinic between 1913 and 1939, and the authors could find no previous references in the literature other than that of Berkheiser. Amongst their 20 cases 3 were classified as possibly being congenital pseudoarthroses. One was in a female child of 2 years with a fracture of the outer third of the left clavicle in whom no previous treatment had been given. There were no symptoms, no operation was carried out, and there was excellent function. The second case was that of a man aged 33 in whom a fracture was apparently detected in infancy: a congenital origin was suggested but not proved. The fracture was in the middle third of the left clavicle and there had been no previous treatment. The only symptom was mobility at the fracture site. A bone graft was inserted and union resulted. The third case was that of a girl of 18 months; again a congenital origin was suggested but not proved. The fracture was in the middle third of the right clavicle. No previous treatment had been given, and again the only symptom was mobility at the site of fracture. Despite the youthful age of the patient a bone graft was inserted and union resulted.

The fourth case in their series was that of a girl aged 8 years who fell in her bath when 2½ years old. The right clavicle was fractured in the middle third. No record of any previous treatment was obtained. Once again the only symptom was the movement at the fracture site. Open reduction was carried out with the insertion of catgut sutures, but the follow-up was insufficient for observation of the final result. All the other cases recorded in the papers consulted were in adults. The case here recorded occurred in a young child.

Case Report

A female child aged 20 months was first seen in the out-patient department on April 23, 1951. She was referred from a welfare clinic because of deformity of the right clavicle (? as a result of birth injury or as a case of cleido-cranial dysostosis). The patient was a healthy child, the firstborn, and her mother was in her twenties. There were no

complications during pregnancy and the presentation was occipital. Forceps had not been necessary, but, after delivery of the head and while the shoulders were engaged, contractions ceased for some minutes. Contractions then started again and the delivery was completed. The child was bottle-fed and she walked at about 1 year. Her grandmother was the first to notice swelling of the right clavicle, when she was about 7 weeks old; at about this time she was seen in a welfare clinic and the mother was advised to leave it alone. A radiograph was not taken.

On examination in the out-patient department a swelling was obvious in the middle third of the right clavicle. On holding the inner and outer sides of the clavicle definite movement was evident in the swelling and a diagnosis of ununited fracture was made. This was confirmed on radiographic examination (Fig. 1). There was no drooping of

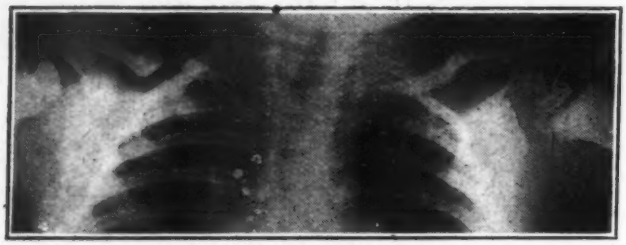

FIG. 1.—Radiograph of Case 1.

the right shoulder, the left clavicle was normal, and there was no scoliosis; no other abnormality was detected on clinical examination.

Owing to the absence of any abnormal symptoms or signs except the presence of mobility at the fracture site, it was debated whether any treatment was necessary. However, it was thought there was a danger that the right shoulder might droop at a later date and that a secondary scoliosis might develop (Professor H. J. Seddon and Mr. St. J. D. Buxton, in personal communications with Mr. Metcalfe). It was therefore decided to insert a bone graft at a later date. Meanwhile the child will be seen for periodical review in the out-patient department.

DISCUSSION

All nine cases recorded by Berkheiser from Chicago in 1937 were in adults and of long standing. Six had brachial plexus involvement and all were caused by very severe trauma. Operative treatment included the use of kangaroo tendon, bone grafts, wire, and heavy braided silk, together with a plaster-of-Paris shoulder spica worn for 12 weeks. Ghormley *et al.* state that in most infants with a fracture of the clavicle the fracture is of the greenstick variety with little or no displacement, and that this is true also of obstetric fractures of the clavicle. Because of the elasticity of this bone, complete transverse fracture with displacement is the exception rather than the rule. None of their cases were of cleidocranial dysostosis. They state emphatically that, despite the aetiology, treatment must be as for the adult, and they recommend massive bone grafting and a period of complete rest in bed for four to six weeks after operation. They add that plaster-of-Paris immobilization does not mean complete local rest unless the patient lies flat.

Annersten (1948), in a review of 350 cases of clavicular fractures seen between 1938 and 1947, records an incidence of 1.3% pesudoarthrosis. All five were adult cases and all followed injuries. He recommends the use of bone chips and wiring, and an aeroplane splint for four weeks after operation. Thorndike (1938) states that the clavicle is the bone most often fractured in obstetric delivery, and adds that birth fractures are not always simple incomplete fractures; this view differs from that put forward by Ghormley *et al.*

Le Cocq and Gilman (1944) record four cases, all in adults and all following injury; they recommend the insertion of a four-screw vitallium plate and subsequently neither rest in bed nor plaster-of-Paris immobilization. Støren (1946) quotes Bohler, on clavicular pseudoarthrosis, as having seen six cases after early instituted energetic passive movements or following operative treatment. This latter view is also suggested by Watson-Jones (1943), who agrees with other writers in advising the use of a bone graft. Støren records the case of a woman aged 39 who had had a left-sided clavicular pseudoarthrosis for 29 years, for 26 of which she had been without pain. Basom *et al.* (1947) recommend dual grafts for non-union. Novotny (1949) states that cases without fibrous or bony union do occur, and he uses his own plaster-of-Paris splint for these cases.

McMurray (1949) states that non-union is comparatively rare, especially when fractures are simple. He says they are seen only when treatment is neglected or when part of the bone has been removed in a compound fracture. He recommends bone grafting, or the removal of a section of the clavicle on each side of the fracture or complete removal of the affected clavicle. It is suggested that in the case recorded here the fracture was probably sustained during delivery and that it may be classed as a birth fracture.

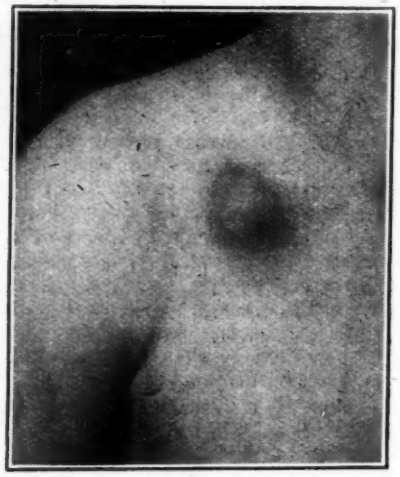

FIG. 2.—Case 2, showing a swelling in the right clavicle.

ADDENDUM.—Since this paper was submitted for publication a further case has been seen at St. James's Hospital. A boy aged 9 presented with a swelling over the middle third of the right clavicle, without any history of injury (see Fig. 2). Clinically there was mobility at the site of the swelling, and the diagnosis was confirmed by a radiograph.

I wish to acknowledge my thanks to Mr. R. H. Metcalfe for his permission to publish this case, to Mr. G. P. Arden for kindly reading this paper for me, to Dr. R. L. Quilliam for his radiographic report, and to Miss E. Mason for the *x*-ray photograph.

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The arrival of autumn has been marked by a meeting in Geneva of World Health Organization experts on influenza. British delegates were Dr. C. H. Andrewes, who directs the W.H.O. Influenza Centre at the National Institute for Medical Research, Mill Hill, and Professor C. H. Stuart-Harris, of Sheffield. The main subjects of discussion were the identification of influenza strains, standard methods of diagnosis, vaccines, the collection and dissemination of epidemiological information, treatment, control measures in severe epidemics (including the place of vaccines and antibiotics), and the training of workers in laboratory methods.

Reviews

HALSTED'S PAPERS

Surgical Papers by William Stewart Halsted. Volumes 1 and 2. (Pp. 1,189; illustrated. £10.) Baltimore: The Johns Hopkins Press. London: Geoffrey Cumberlege. 1952.

The reprinting of the surgical papers of William Stewart Halsted on the occasion of the Halsted Centenary Celebrations at Baltimore earlier this year constitutes an important surgical event. The original volumes had long been out of print, only well-thumbed and tattered copies in medical libraries or treasured possessions of individual surgeons being available. The publishers have retained the format and the complete contents of the original printing, including the striking introductory appreciation of Halsted by Matas with its quotation from René Leriche, for whom Halsted was one of the great formative surgical influences. The collection starts with Halsted's first paper in 1883 on "Refusion in the Treatment of Carbon-monoxide Poisoning," and concludes with his epoch-making address on "The Training of a Surgeon." The former illustrates how from the very beginning a bold and original mind applied itself to the problems of surgery; and Halsted's advocacy of centripetal arterial transfusion has to-day a peculiarly modern ring. The paper on the training of a surgeon, though based on an address delivered at Yale in 1904, is a fitting conclusion to the volumes, as representing perhaps the main continuing influence of Halsted on surgery. In between we have a wealth of papers on the breast, thyroid, blood vessels, hernia, the intestines, surgical pathology, surgical experimentation, and surgical technique, as well as on regional local analgesia, of which he was the discoverer.

The most striking impression on rereading these papers is the freshness of their point of view, often 50 years or so after they were written. Thus, in reading the breast paper of 1898, one is struck by such sentences as, "Dr. H. W. Cushing, my house-surgeon, has in three instances cleaned out the anterior mediastinum on one side for recurrent carcinoma. It is likely, I think, that we shall in the near future remove the mediastinal contents at some of our primary operations." Halsted does not appear to have followed up this line of thought, and it was left to R. S. Handley to bring to fruition the work of his father, Sampson Handley, by demonstrating quantitatively the importance of the internal mammary gap in breast cancer. But Halsted was clearly approaching the fringes of a problem—the closing of the internal mammary gap—which is the most immediate one facing surgeons and radiotherapists to-day in the treatment of breast cancer. Similarly striking are the hernia papers, and it is often a rewarding and sometimes chastening experience for surgeons developing a new idea in hernia surgery to make sure that Halsted has not already anticipated them. For example, the statement, "The internal oblique muscle, mobilized, and possibly further released by incising the anterior sheath of the rectus muscle, is stitched to Poupart's ligament," embodies an idea which has often been rediscovered as new. In view of the great influence of Blalock, Halsted's present great successor at the Johns Hopkins Hospital, on the development of modern cardiovascular surgery, Halsted's papers on this subject, though primitive by modern standards, have a special interest. It is interesting to note, for example, the combination of the practical, the theoretical, and the experimental, and the constant returning to the subject of the cause of dilatation of an artery beyond a constriction. Halsted solved very few cardiovascular surgical problems, but his legacy to the Hopkins was a habit of thought and experiment which has led to key solutions.

Much of what Halsted wrote must naturally now be outdated by the progress of surgery, and even his ideas on the training of a surgeon may need recasting in the light of the revolutionary changes in the relation of hospitals to the community, in America no less than elsewhere. But few collected surgical papers could so well illustrate the fertilizing influence of great ideas by a great man who was fortunate in the time and country of his birth and activity, or so well serve as a text on the value of the combined scholarly-historical and progressive approach to surgery. All medical libraries will have to possess these collected papers of Halsted, and there is no doubt that many individual surgeons will decide that the high cost of American medical publications in this country since the devaluation of the pound will this time have to be paid.

DAVID H. PATEY.

KIDNEY INNERVATION

The "Neurility" of the Kidney: A Monograph on Nerve Supply to the Kidney. By C. G. De Muylder, M.D. With preface by Professor Joseph Trueta. (Pp. 80; 46 figures. £1 5s.) Oxford: Blackwell Scientific Publications. 1952.

This is a curious book with a curious title. Neurility, according to the dictionary definition, is the ability of a nerve to convey stimuli. This suggests a physiological dissertation, but the book is, according to its own subtitle, a monograph on the "nerve supply to the kidney," and in the preface the author states that it is concerned with the anatomy of the renal nerves. Yet he starts off with the dubious premise that nothing need be said about the macroscopic innervation of the kidneys, and some of his subsequent remarks reveal that he is unfamiliar with the various origins and routes of the renal nerves.

The first section of the book is on the intrinsic distribution of renal nerve fibres. No exact details are supplied about the number or nature of the specimens examined, but apparently many of the observations were based on foetal mice. The story is neither complete nor particularly convincing, and, although the drawings of nerve fibres and endings are excellent, most of the supporting photomicrographs are less good. Dr. De Muylder failed to discover evidence of tubular innervation, a finding at variance with most previously published observations, but he was impressed by the profuse nerve supply of intrarenal arteries and by the occurrence of "intravenous" endings in veins. He states, without offering any real proof, that most of the renal fibres are sympathetic and vasomotor, and probably regulate the blood flow through axon reflexes. He quotes, without criticism, opinions implying that "intravisceral (digestive) nerve cells" are sympathetic; and he seems to accept, without considering other possibilities, that neural crest cells give rise to sympathetic ganglia and that nerve cells in the intestinal wall and lungs are derived from the same source.

A substantial part of the monograph is devoted to the juxtaglomerular apparatus, and a series of somewhat confusing observations and deductions linking it with "mesectoderm of neurectodermic origin." Finally, an attempt is made to correlate the renal innervation and concepts of the juxtaglomerular apparatus with renal pathology and physiology. These sections can only be described as sketchy and speculative. Some of the conjectures are possibly correct and they may provide ideas for other workers in this field to pursue, but they fail in this presentation to measure up to the standards set even by a moderate exercise of the *scepsis scientifica.*

G. A. G. MITCHELL.

CANCER OF THE RECTUM

Traitement Chirurgical du Cancer du Rectum. By F. d'Allaines, A. Le Roy, N. du Bouchet, Ch. Dubost, J. le Brigand, and J. Vaysse. Second edition. (Pp. 246; 76 figures. 5,750 francs.) Paris: Éditions Médicales Flammarion. 1951.

The second edition of Professor François d'Allaines's well-known monograph on the surgical treatment of cancer of the rectum has now appeared. The interval of four years since this work was first published has enabled a larger series of operations to be recorded, and the book has been considerably enlarged; new sections on pre-operative preparation and anaesthesia have been added. The same well-known and beautifully clear illustrations depicting surgical technique that we saw in the first edition (some slightly modified) are shown again and give detailed help and guidance to any

surgeon who wishes to perform conservative or restorative operations for rectal cancer. It is clear that the author's preference is for the abdomino-sacral operation, and two methods of terminating this are shown, one by a pull-through manœuvre, the other by circular rectorrhaphy via the sacral incision. The Hochenegg or Babcock–Bacon operation has not appealed to d'Allaines; on the whole he considers that rectal function is indifferent after this operation, which he now reserves for very small tumours situated 8–10 cm. above the anus; his experience of the Babcock–Bacon procedure extends to 53 cases.

The chief interest in this book will be found in the preliminary anatomical and statistical argument in favour of restorative operations (p. 64), but one item here requires comment. In a series of 239 resections a mortality of 6.7% within 15 days is reported, whereas in a series of 101 radical amputations the mortality was 20%. But this is hardly a just comparison, for in most clinics the modern operative mortality for combined excision of the rectum is less than 5%. It is interesting to note that in the entire series 66% were treated by a restorative operation, and in the last two years this figure has risen to 75%. The author states that he has never seen a perineal recurrence after resection of a cancer of the pelvic portion of the rectum. The indications for anterior resection of the rectum are discussed, and rather than be obliged to carry out a wide dissection of the sub-peritoneal space and a low anastomosis below the cul-de-sac of Douglas he prefers the abdomino-sacral route as being easier and more certain. So far as survival rate is concerned d'Allaines reports 50% five-year survival after abdomino-sacral resection (32 out of 64 cases) with 12 local recurrences, of which 9 were in the pelvis and three in the conserved part of the rectum. Many other items other than those mentioned are worthy of careful study, especially the author's remarks on anastomotic strictures and faecal fistulae.

The work is one which will, we feel sure, continue to serve as an important and authoritative guide to surgeons who propose to embark on these operations. An up-to-date bibliography is given at all its stages. Professor d'Allaines and his associates have made an extensive and impartial study of the subject for which surgeons the world over will be grateful.

W. B. GABRIEL.

DEVIATIONISM IN PSYCHIATRY

Academy of Sciences of the U.S.S.R. Scientific Session on the Physiological Teachings of Academician I. P. Pavlov. June 28 to July 4, 1950. Inaugural Address, Reports, Resolution. (Pp. 174. 2s. 6d.) Moscow: Foreign Languages Publishing House. London: Collet's Holdings Ltd. (45, Museum Street, London, W.C.1). 1952.

The programme of this session was to expose, "in the spirit of criticism and self-criticism . . . the serious errors and shortcomings in the elaboration of Pavlov's scientific legacy." Short addresses by the president and vice-president foreshadow the atmosphere of the congress as a whole: there is only one road in physiology and its application to medicine, the road mapped by Pavlov, and it has not been followed satisfactorily by the Russian scientists of to-day.

The bulk of the book consists of a report by K. M. Bykov and Ivanov Smolensky on Pavlov's work and a criticism of those Russian scientists who have deviated from his teachings. The general survey of Pavlov's work deals with his study of conditioned reflexes, his investigations into the interrelations between external and internal factors leading to his theory of "nervism." In Pavlov's opinion the equilibrium between external and internal processes is organized by the cerebral cortex. There is no single function of the body which is not controlled by higher levels of the C.N.S., and there is a unity of all levels of the nervous system. Pavlov discounts the theory of separate associative centres and the existence of any special part of the hemisphere possessing a supreme nervous function. He postulates, however, two signal systems in the cortex—a first system which regulates the vegetative reactions and behaviour, and a second for verbal activity.

Much of the space of the two speakers is devoted to an attack on Western dualistic, idealistic, and mechanistic theories and on leading Russian scientists who are suspected of deviationism in this direction. There is a ban on Sherrington's work, on the German school of "cerebral pathology," and on Freudian ideas; psychosomatic medicine is considered to be based on reactionary theories "in order to defend the interests of the ruling class." Among the Russians found guilty of one or the other of the Western heresies were I. S. Beritov, Stern, Speransky, and Gurevich.

The closing speeches were again delivered by Bykov and Ivanov Smolensky: they reveal the already familiar pattern of publicized scientific discussions in the Soviet Union. No mercy was shown to the deviationists in spite of their self-accusations and recantations.

There is little point in criticizing or in arguing about the methods and dialectic of scientific discussion in the Soviet Union. It is not surprising that Pavlov's materialistic conceptions have been enthroned as scientific law in the U.S.S.R. But one wonders what the Russian authorities had in mind in publishing a translation of these proceedings, which cannot but antagonize the scientists of the English-speaking world, however much they appreciate Pavlov's great contribution to knowledge.

R. KLEIN.

HISTORY OF DIABETES

The History of Diabetes Mellitus. By N. S. Papaspyros. (Pp. 100; 10s. 6d.) London: H. K. Lewis. 1952.

Dr. Papaspyros has put together a useful history of diabetes and glycosuria, tracing the knowledge of the disease step by step. In a very extensive investigation of sources he has brought to light many links in the historical chain that were obscure or unknown even to professional historians. It is a pity that he did not have his work looked over by a literary reviser, for his narrative is sometimes disjointed and ill-arranged.

It is remarkable, as he points out, that diabetes is not recognized in the writings of the early Greek physicians, the more so in that it is unmistakable in the Indian Vedic literature. It was, however, mentioned by the later Greek physicians. Knowledge of the pancreas was set forth by Galen in the second century A.D., though he does not connect it with diabetes. Despite valuable experiments and observations in the seventeenth and eighteenth centuries and the magnificent work of Bernard in the nineteenth, it was not until 1889 that diabetes was caused experimentally by removal of the pancreas. The discovery of the islets of Langerhans in 1869 was on a purely structural basis, and knowledge of the metabolism of the diabetic state was not understood until Naunyn expounded it in 1898. The work of Banting and Best, begun in 1921, led to a true linkage of structure and function of the pancreas. The history of this process has been related by Banting himself. The change in outlook introduced by these discoveries was so rapid that in 1925 Dr. R. D. Lawrence was able to write in the preface of his *Diabetic Life*, "Five years ago *Diabetic Death* would have been a more suitable title for such a book than *Diabetic Life*."

CHARLES SINGER.

Nurses' instruction in anaesthesia in many hospitals is still limited to a perfunctory lecture from the senior anaesthetist and a demonstration by the sister tutor of largely out-of-date apparatus. Yet the modern patient, with his physiology balanced between the effect of one poisonous drug and another which is its antidote, is regularly abandoned by the specialist in anaesthesia to a junior ward nurse and a pair of wholly untrained orderlies: the road back to bed is a dangerous one. A book about anaesthesia for nurses was undoubtedly needed, and Dr. W. J. Finnie has gone a long way to producing a useful one (*Anaesthetics and Anaesthesia for Nurses*; London: The Nursing Mirror Ltd.; 7s. 6d.). He writes simply and shortly about pre-operative care, anaesthesia, and anaesthetic apparatus, but his book would be much more useful if he emphasized the nurse's duty towards the unconscious patient, and post-operative hazards—for example, an obstructed airway—at the expense of such information as a description of refrigeration analgesia.

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CENTENARY OF WILLIAM STEWART HALSTED

Surgery, both as a science and an art, grows normally by innumerable and imperceptibly small improvements. Each is usually contributed by some able practitioner, known in his own circle and time, but seldom commemorated, famous, or even remembered far beyond. The details of procedure on which the successful daily prosecution of surgery depends are almost necessarily matters of example and tradition, the minutiae of which can hardly be included in even the fullest treatise on the subject. Thus only very few of the great surgeons of the past are often mentioned in the modern operating theatre. Among them is certainly William Stewart Halsted (1852–1922). He is perhaps most often spoken of in connexion with the technique of the operation for the removal of the breast and its associated lymph glands and his modification of the operation for hernia. But Halsted was much more than a designer of operations. He was, beyond doubt, one of the founding fathers of twentieth century surgery, a great and inspiring teacher, and a surgical thinker of the first rank.

Halsted was born in New York. His career at Yale University was distinguished only by athletic achievements, but he graduated in medicine in 1877 from the College of Physicians and Surgeons (Columbia) with a fine scholastic record. After resident appointments, during which he came under the all-pervading influence of W. H. Welch, he spent two years in German and Austrian universities. The period was the most hopeful in the history of German medicine. Bacteriology, pathological anatomy, histology, embryology, and chemical pathology were advancing rapidly. They had all become almost German sciences. This was largely the result of the rich endowment of German research institutes, which were as yet without parallel elsewhere. On his return to New York in 1880 Halsted was at once accepted as a leading surgeon. For six years he conducted an extremely active hospital and private practice and attained high distinction both as a teacher and as an investigator. Of all his work during these years perhaps the most important and permanent was that on the use of cocaine. In 1884 Karl Koller reported the anaesthetic properties of the drug on the cornea at a meeting of the German Ophthalmological Society at Heidelberg. Halsted's work on cocaine began in 1885, and it greatly extended both the knowledge of the drug's action and its practical application. He demonstrated the advantages of injecting it into the dermis rather than hypodermically, and the prolongation of its effect when the circulatory activity of the part was reduced. Above all, he proved its regional analgesic effect when infiltrated into a sensory nerve. This work was epoch-making for surgery and dentistry, but its immediate effect was disastrous for Halsted himself. Knowing nothing at that time of the habit-forming nature of cocaine, and experimenting frequently on himself, he became an addict. He was cured only by a long course of hospital treatment, which left considerable but not wholly undesirable marks on his character.

In 1886 he joined Welch at the Johns Hopkins Medical School and became surgeon to its hospital, opened in 1889. He now became associated with Osler, Mall, Walter Reed, Abbott, Simon Flexner, and Councilman. The last wrote of him: "Halsted proceeded to work on the basic question of operative procedure and the treatment of wounds. He read all the old papers of Lister and carried out all the methods which he gave experimentally on animals, but with a more thorough study of the results than would have been possible when Lister did his work, for by 1886 the science of bacteriology had been developed and reliable methods of work established. The methods of Lister were complicated, and involved the use of materials which were difficult to procure. Halsted showed that cultures made from wounds, treated after the most meticulous use of the Lister methods, showed the presence of bacteria on the surface. This led him to a careful microscopic study of wounds and to the realization that care in operating, the exact approximation of surfaces, and the avoidance of dead spaces, were as important for results as the supposed avoidance of bacteria. . . . The study of hand disinfection was no less thorough, and this led to the realization that the hands could not be sterilized, and finally to the use of rubber gloves in operating. . . . It is difficult to think of surgery more carefully conducted than was this experimental surgery of Halsted. . . . Probably not since the time of John Hunter had experiment been so fully utilized in the development of surgery."

The first 15 years after the opening of the hospital were the most productive of Halsted's life, which became entirely different from that which he had led in New York and in the pre-cocaine era. He was a completely new man. From being a busy surgeon

with many appointments and acquaintances, he became now a quiet scholar and experimenter who sought seclusion, save for his earnest teaching. As a surgeon he was no longer a rapid, spectacular operator but rather an extremely careful though not unduly slow one. Intestinal suture and the healing processes of wounds were among his objects of study. In technique he improved or developed operations for hernia, thyroid disease, aneurysm, and especially carcinoma of the breast. Meanwhile he made frequent trips to Europe and developed a lifelong association with and affection for the brilliant and modest Swiss surgeon Theodore Kocher, of Berne. Among the best known of his many pupils were Cushing, Bloodgood, and Mitchell.

The later years of Halsted's life were given to establishing methods of clinical teaching and to training other surgeons. In these tasks he was quite extraordinarily successful. He had about 238 resident surgeons under him during his period of office. Of these some 140 became academic instructors in surgery. Truly, surgery as practised now in the United States is the child of William Stewart Halsted.

ACCIDENT PRONENESS

Penrose[1] has shown that the course of literature on new medical treatments is something like an epidemic—a slow onset of the idea, followed by praise increasing to saturation point, followed by articles against, and eventually declining to cautious statements in medical textbooks. The literature on accident proneness illustrates this. The epidemic has not been severe, comparatively few people have been affected, and the arguments for and against are characterized by moderation. This may be due to the scientific accuracy with which Greenwood and Woods[2] originated the concept in 1919. Their work, and the work of Greenwood and Yule[3] and Newbold,[4] set a standard of statistical precision such that Arbous and Kerrich[5] can only say (even though they doubt whether accident proneness has been demonstrated), "It is a very unfortunate but real fact that our knowledge of this concept has hardly proceeded further, and in some respects has suffered a set-back from the time when Greenwood, Woods, Yule, and Newbold undertook their classical studies in 1919 and 1926." This is a slight exaggeration, but certainly the development has been slow.

Accidents are an important cause of death, disability, and economic loss, and attempts to understand their problems are welcome. But (again to quote Arbous and Kerrich) "data associated with this problem are extraordinarily complicated, and the relationship between causes so intricate, that it is difficult to set up adequate conditions of experimental control, and to isolate the various determining causes." The main difficulties are, first, in obtaining reliable evidence; secondly, in defining and measuring accident proneness; and, thirdly, in relating the measured accident proneness to other medical or psychological qualities of the individual.

The demonstration of individual differences in a group of people requires that as many as possible of the conditions to which they are subject be kept constant. A number of people should work the same amount of time in identical conditions on identical work. Further, they must have sufficient accidents to provide evidence—however accidents may be defined. These conditions cannot be completely fulfilled, for factory work changes; people go off sick or are absent as a result of an accident. To minimize these difficulties Greenwood and Woods worked with minor injuries only—not injuries causing loss of time—and kept their observation periods short. Their defence of this procedure was that "the law of a *distribution* will not in general be affected by the consequences attaching to the results. The number of sixes thrown with a pair of true dice in a hundred trials will not be affected by the height of the stakes." While this is sound statistics it is not necessarily good psychology, and people have accidents, not dice. Adelstein[6] found little correlation between major and minor accidents, thus confirming the work of wartime investigators. There is also the possibility when investigating accidents that what is being examined is proneness to report accidents—not proneness to experience them. The criterion of an accident itself provides a difficult problem, with no real solution other than that of expediency (such as compensation criteria).

The statistical demonstration of individual difference is usually performed in any of the following three ways: departure of the observations from chance distribution may be tested; the recording period may be split into halves to see what would have happened in the second half had the worst members of the first half been removed; and the observations in the two half periods may be examined for correlation.

To perform any of these tests adequately needs a good deal of evidence—a large number of people and many accidents—and care must be taken to ensure that the population has as homogeneous an experience as possible. But these conditions are rarely achieved, and chance plays a large part in the obser-

1 *On the Objective Study of Crowd Behaviour.* H. K. Lewis. 1952.
2 *Rep. Industr. Hlth Res Board (Lond.)*, 1919, **4**.
3 *J. roy. statist. Soc.*, 1920, **83**, 255.
4 *Rep. Industr. Hlth Res Board (Lond.)*, 1926, **34**.
5 *Biometrics*, 1951, **7**, 340.
6 *J. roy. statist. Soc.*, to be published.
7 *Rep. Industr. Hlth Res. Board (Lond.)*, 1926 *et seq.*, **38, 55, 68, 74, 84**.
8 *S. Afr. Air Force J.*, 1949, **1**, 2.
9 "Pilot Errors," Air Ministry 3139 A., H.M.S.O., London.
10 "Accident Proneness in Coal Miners" (unpublished communication).

vations. This is best illustrated by a fictitious example. Suppose there are 1,000 men, all engaged on identical work under identical conditions, and that 900 have a true risk of one accident a year, and 100 have a true risk of two accidents a year. These are conditions which would favour the discovery of accident proneness. The records are treated in the usual ways. Six months would reveal nothing; neither would a year. Two years' records give rise to suspicion, and after three years there would be sufficient evidence to say that the individuals were not all the same so far as accident liability is concerned. Thus even in these ideal conditions the progress of investigation would be slow. If at the end of three years we picked out the 70 men with seven or more accidents, we could have 39 prone and 31 normal. Correlational procedures would not be very helpful, two one-year periods yielding a correlation of +0.076, two two-year periods +0.141, and two three-year periods +0.197. If it were possible to correlate two 10-year periods the value would leap to +0.450. Thus it is hardly surprising that analysis of data with smaller numbers and with shorter exposure periods often fails to demonstrate accident proneness. What is more surprising is that doubt is then cast on the hypothesis rather than on the evidence.

The work of Farmer and Chambers[7] and of Biesheuvel,[8] and the more clinical investigations by Davis,[9] show (despite the difficulties of measuring accident proneness) that accident proneness is associated with other qualities of the individual. Farmer and Chambers showed that aestheto-kinetic performance tests could predict the chances of accident proneness in a person, though perhaps not sufficiently strongly to warrant application. Biesheuvel in South Africa (using a mixed battery of tests) and Davis in this country showed that it is possible to predict which pilots are likely to have flying accidents. The wartime work departed from the idea of a single personal quality of accident proneness. Instead accident proneness was regarded as the behavioural consequence of a number or constellation of personal qualities. Biesheuvel suggested various accident "indicators," and based his predictions on the total number shown by the individual. Davis showed two distinct patterns of flying breakdown, and related these to psychopathology. More recently Whitfield[10] has suggested that accident proneness can be attributed either to perceptual or to motor failure.

Less can be said about the practical application of the knowledge gained. These studies inevitably raise the delicate issue of personnel selection. It can possibly be held that, for occupations involving responsibility for the safety of others—such as piloting aircraft—the use of any and all evidence to select the least accident-prone individuals is a necessity. For industrial populations such a procedure would be cumbersome and wasteful and, in the present state of knowledge, unjustified. It will probably prove more profitable in the long run to discover more about the conditions giving rise to accidents and about the limits of perceptual and motor response of the average person, so as eventually to modify the working environment and reduce the total risk, rather than to pick out the unfortunate accident prone.

EUROPEAN CONGRESS OF CARDIOLOGY

Over 500 medical men and women from European countries and the United States attended the meetings of the First European Congress of Cardiology, held last week at the University of London from September 9 to 12. A total of 88 papers were read at the Congress, and over two-thirds of these were on mitral valvular disease and electrocardiography. It is interesting that hypertension and cyanotic congenital heart disease, which a few years ago would have occupied a large part of the programme, received relatively little attention, and the treatment of heart disorders, apart from the treatment of mitral disease, was discussed in only four papers.

One morning was devoted to a symposium on mitral valvular disease, and the same topic was discussed in two other sessions. There was general agreement that the results of mitral valvotomy were good or excellent in three-quarters of the cases operated on and that the operative mortality was low in those cases with pure mitral stenosis. Even in patients with auricular fibrillation, aortic valvular disease, or greatly enlarged hearts the immediate results were good although the operative risk was much greater. Several speakers described the changes in the pulmonary circulation before and after valvotomy. Before operation a moderate rise in the resting pulmonary artery pressure was the usual finding with a further increase after exercise. A large fall in pulmonary artery pressure was common after valvotomy, although the maximum haemodynamic improvement might not be reached until a period of six to nine months had passed. Subjective improvement was immediate, and the increased effort tolerance probably provided the best measure of the success of the operation. The magnitude of the task confronting cardiac surgeons was emphasized: one speaker calculated that 4,000 cases a year would have to be operated on in this country alone, so that many new centres would be needed.

There was general agreement among speakers at the Congress that it was impossible to assess accurately the amount of mitral incompetence which was present in patients with mitral stenosis. Tracings of pulmonary capillary pressure, which closely paralleled changes in left auricular pressure, failed to give reliable information on this point. This is not surprising, since direct pressure readings from the left auricle before valvotomy in proved cases of mitral incompetence sometimes fail to show diagnostic changes. A small series of cases was reported in which a pericardial sling had been introduced to lessen the degree of mitral incompetence; the

results seemed to justify further study. Pure mitral incompetence is rare, but, as some speakers reported, might be diagnosed with some confidence if the mitral first sound was soft and there was a loud systolic murmur at the apex, often conducted to the axilla and back, the murmur being accentuated in late systole. The opening snap of the mitral valve was not heard in mitral incompetence.

The use of multiple leads in electrocardiography has greatly aided the accurate diagnosis of myocardial infarction, and although several speakers described additional leads other than the conventional chest and limb leads it seemed that these provided little additional information. Vectorcardiography has still to establish its place as a useful routine examination, but in several papers results of great theoretical interest were reported. The success of this first European Congress of Cardiology was undoubted, for in addition to the scientific programme it provided a most useful opportunity for discussion between physicians from most of the countries of Europe.

FOOD-POISONING FROM COCKLES

Cooked cockles, prawns, and shrimps are sold in great quantities during the summer season in the towns of the Thames estuary. The occurrence in these towns of over 400 cases of food-poisoning in three successive week-ends during the autumn of 1949 drew attention to problems of hygiene connected with the sale of the shellfish, for there was no doubt that these were the vehicles of infection.[1 2] Cooked shellfish of course do not present the obvious risks associated with oysters and mussels, which are usually eaten uncooked and may be infected with typhoid bacilli or other enteric pathogens derived from polluted water. The cockles, which are the chief source of trouble, are harvested from the sands of the Thames estuary with steel rakes and steamed for six minutes in cooking-pots. The fish are then passed through a riddle to free them from the larger pieces of shell, and transferred to a series of tanks of water, where they are stirred to get rid of smaller debris. They are then heavily salted for transport to more distant markets, but only salted to taste for local sale. Food-poisoning was traced only to the lightly salted cockles. Most of the victims had a short, sharp attack of diarrhoea and vomiting, beginning 3 to 72 hours (average 16 hours) after eating the shellfish. Recovery was rapid, and no deaths were reported.

Bacteriological examination showed that the cockles are sterilized by the steaming and that the infection is due not to the recognized enteric pathogens but to massive dosage with the "borderline" pathogens such as proteus, coliform bacteria, and viridans streptococci. There is ample opportunity for contamination with these organisms during the washing process and while the fish are being arranged for sale in the shops and on the stalls. Precise epidemiological investigation is difficult because of the peripatetic habits of the day tripper, who is the usual victim, and his customary wide range of dietary experiments, though he will generally blame the shellfish for any internal upset. The hawker in a small way of business who quickly disposes of his stock is probably less suspect than the shopkeeper whose large heaps of fish are displayed and repeatedly handled under conditions which favour enormous bacterial proliferation in warm weather. At the time of the outbreaks the weather was dry as well as warm, and dust probably contributed its quota of bacteria.

Public health control is complicated, since the collection and cooking of the shellfish are supervised by the port health authority under the Public Health (Shellfish) Regulations, 1934, and the later stages of their preparation for sale are the concern of the local authority under Section 13 of the Food and Drugs Act, 1936. There are powers to provide for the prohibition of sale of shellfish which, after sampling, are considered likely to cause food-poisoning. Since no one source was consistently implicated during the Thames estuary outbreak and suspect stocks had all been disposed of by the time cases were reported, conditions justifying action never existed.

A modification of the methylene blue test for ice-cream and tests for the detection of *Bact. coli* have been studied in the hope of devising bacteriological standards below which samples of shellfish from producer and retailer should not fall. These investigations are to be the subject of a later report. Meanwhile observations during the last two seasons have shown that much can be done to improve matters by applying the common rules of hygienic food production, including the extended use of refrigeration. The ideal would be to devise a commercially acceptable arrangement by which the shellfish were cooked sufficiently to facilitate removal of the shell, washed to separate other debris, and finally cooked to sterilize them.

[1] Logan, J. S., and Oliver, J. O., *Mon. Bull. Minist. Hlth, Lond.*, 1952, 11, 123.
[2] Pilsworth, R., ibid., 1952, 11, 128.

FIGURES AND 'FLU

Epidemiologists have for some time realized that the weekly figures of new claims for National Insurance benefit may bring to light some interesting facts. Normally the claims vary only within relatively narrow limits: as would be expected, they are rather higher in winter than in summer. The third annual report[1] of the Ministry of National Insurance shows how the claims rose to many times the normal number during the 1951 epidemic of influenza A. Taken together with mortality statistics and other information, the figures suggest that influenza A was directly or indirectly responsible for almost all this big increase. Such information can give a very rapid indication of the onset of an influenza epidemic. It seems also that, treated geographically, it can teach us much about the spread of an epidemic. Eight maps of Great Britain in the report show the amount of rise above normal of the new claims week by week. They began to increase in mid-December, 1950, in Tyneside and Aberdeen, also in the Shetlands and East Anglia—all areas having direct communication with Scandinavia, where influenza had broken out a month or so earlier. Shortly afterwards another focus, since dis-

[1] Third Report of the Ministry of National Insurance for 1951, Cmd. 8615, H.M.S.O., London.
[2] Isaacs, A., and Andrewes, C. H., *British Medical Journal*, 1951, 2, 921.

covered to be associated with a serologically different strain of virus,[2] appeared on Merseyside. There was yet another plague-spot, in Cornwall, which seems not to have led to much trouble. By the first week of January the new claims were at least twice the normal over the whole country except for Skye. The more vicious virus in Liverpool was causing greater morbidity there than elsewhere; the maps suggest that this virus spread during the next week or two to other parts of Lancashire and over almost all North Wales, also to a few areas of south-west Scotland. The same type of virus was prevalent in Northern Ireland at this time. After a very few weeks of high figures, the new claims began to drop back to normal, doing so first in Aberdeen and Tyneside, where they had first risen. By mid-February they were back to normal over almost all the country. It is a pity there is not more information available about the parts played in different areas by the mild Scandinavian virus and the fiercer Liverpool one. Apart from that, the maps contain much food for thought. The spread all over Britain between the week ending January 2 and that ending January 9 was phenomenally rapid: it is hard to believe that any transference due to ordinary man-to-man contact could have proceeded with that speed. Naturally thoughts arise of pre-seeding of virus and an all but simultaneous activation of that widely scattered seed. On the other hand, the start of the epidemic around east coast ports most apt to be infected from Scandinavia induces quite a different train of thought. There is something odd here waiting to be found out. In any case the "new claims" tool seems likely to be a useful one for applying to such problems.

TREATMENT OF PERNICIOUS ANAEMIA

The evidence now available indicates that lack of vitamin B_{12} is responsible for the anaemia in Addisonian pernicious anaemia: the vitamin is not absorbed because of the gastric lesion present in this disease. The observation that vitamin B_{12} behaves both as the extrinsic factor and as the anti-anaemic principle of liver has been confirmed. The content of the vitamin is far lower in the tissues of untreated patients than in corresponding tissues from normal individuals, but the serum concentration approaches normal after therapeutically effective doses of the vitamin or of liver extract have been given.[1] Taken in conjunction with the uniformly excellent clinical and haematological responses, and improvement in the neurological signs if present, these findings suggest that the disease may be effectively treated by crystalline vitamin B_{12} alone.

In a recent issue of this *Journal* Blackburn, Burke, Roseman, and Wayne[2] reported the results of such treatment over a period of two years. Twenty-two of their 60 patients had been treated with liver extract before changing over to vitamin B_{12}, and comparison of the two methods of treatment was thus possible. The authors found that, provided adequate amounts of the vitamin were given, the general condition of these patients was at least as good as when they had been treated with liver extract, and their blood counts were significantly higher. As these authors, and Ungley,[3] observe, this experience is shared by most haematologists in this country. The results of the Sheffield writers go a long way towards justifying their advice that the disease should be treated by injection of the vitamin rather than by liver extract. The findings of Girdwood and Carmichael[4] provide further justification, for they reported that the activity of numerous batches of British liver extracts could be accounted for by their vitamin-B_{12} content, as estimated microbiologically.

Patients vary greatly in their requirements for the vitamin, and the closest clinical and haematological control of the treatment is still of course essential. There is also a great difference between the amount of vitamin B_{12} which will maintain patients in a state of reasonably good health—without severe neurological relapse, and with red cell counts between 4 and 4.5 million—and the amount required to maintain them in excellent health—free from even infrequent episodes of glossitis and paraesthesiae, and with the red cells completely normal in both number and size. In last week's *Journal* Drs. W. Walker and R. B. Hunter[5] emphasized that patients in the earliest stages of relapse may become deficient in the vitamin some time before there are any changes in the peripheral blood.

The available evidence, recently reviewed by Ungley,[3] suggests that a dose of 50–100 μg. of the vitamin every fortnight will restore the blood count of most patients to normal, though larger doses are probably required for the treatment of patients with neurological signs. Blackburn and his colleagues in Sheffield advised the injection of at least 50 μg. a fortnight for maintenance. Since highly concentrated solutions of the vitamin are now available it is possible to give large doses in a short time, and it would therefore seem reasonable during the first few days of treatment to give enough to replenish the depleted body stores. Wolff and his colleagues[6 7] have estimated the normal content of the vitamin in liver and found that in pernicious anaemia the amount was reduced to a tenth, while Girdwood[8] observed complete absence of vitamin B_{12} from the tissues of an untreated case. It has been suggested that the body normally retains about 2 mg. of the vitamin, and since about half the dose after large injections is lost by excretion the total dosage needed to restore reserves would ordinarily be about 5 mg.

Though it seems justifiable to assume that the primary deficiency in pernicious anaemia is a lack of vitamin B_{12} and that there is nothing to be gained by treating patients with refined liver extracts, certain questions still remain unanswered. Norwegian workers[9 10] have found a persistent macrocytosis and a persistently increased prothrombin time in some patients treated with refined extracts and with vitamin B_{12}, but not in patients treated with crude liver extracts. These observations have not yet been confirmed in this country, but further information on this point is still urgently required.

1 Mollin, D. L., and Ross, G. I. M., *J. clin. Path.*, 1952, **5**, 129.
2 *British Medical Journal*, 1952, **2**, 245.
3 *Nutr. Abstr. Rev.*, 1951, **21**, 1
4 *British Medical Journal*, 1950, **2**, 1357.
5 Ibid., 1952, **2**, 593.
6 *C.R. Acad. Sci. Paris*, 1951, **232**, 568.
7 *Bull. Soc. méd. Hôp., Paris*, 1951, **67**, 281.
8 *Biochem. J.*, 1952, **52**, 8
9 Larsen, G., *Proceedings of the Third International Congress of the International Society of Haematology*, p. 25, New York, 1951.
10 Owren, P. A., ibid., 1951, p. 34.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

NEPHRITIS—II. PROGNOSIS AND TREATMENT

BY

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Prognosis in Type 1 Nephritis

In prognosis we quickly become aware that what may be significant to the statistician is quite inadequate for the clinician, who is called upon to deal with individuals rather than "populations at risk." What the parents of a child with acute nephritis want to know is not the overall recovery rate but whether their particular child is going to be in the 80% who recover or the 20% who do not. Of course it is important for both doctor and relative to know that the general chances of recovery are high, but by taking note of the course of events in the individual we can often go a good deal further.

Cases with an acute onset, however ill in the first stage, even with convulsions and anuria, often make a complete recovery. Severity of onset is certainly no indication of bad prognosis. Very often, after about a week or a fortnight of oliguria and oedema, there is quite a sudden change for the better. The urine volume, which may have been only 300 to 500 ml., suddenly increases, the oedema rapidly subsides, the puffy bloated appearance of the face disappears, the haematuria and albuminuria become rapidly less. If this happens as a definite and sudden change the prognosis is undoubtedly good and the doctor is fairly safe in saying that all will be well. If a few days later the blood pressure has also returned to normal (for instance, the diastolic pressure is 75 mm. or below) then the good prognosis amounts practically to a certainty. It matters not that some small amount of protein (say 0.5 g. per litre or less) remains in the urine for weeks or even for many months in some cases.

Conversely, if the oedema is slow to clear and after several weeks the patient has still a notable albuminuria (say 3 to 10 g. per litre) and his diastolic pressure is 90 to 100, a progressive and unfavourable course is likely. Recurrence of oedema at this stage usually indicates that the course will be rapidly progressive, with death within two years.

At a somewhat later stage, when the patient has apparently recovered but still has some albuminuria, the diastolic pressure and the amount of the proteinuria are still the best guides. If the diastolic pressure is still raised several months after the acute attack the chronic latent course will almost certainly ensue.

Acute nephritis very rarely recurs despite what the textbooks say. When recovery is complete and albuminuria has entirely ceased, no doubts about the future should be allowed to cloud the mind of the patient or his relatives.

In the latent stage the eventual progression to renal failure is inevitable, but the prognostic art is still important in deciding how long it is likely to take. Not that the information will necessarily be communicated either to patient or to relative, but it will influence the doctor's advice in helping the patient to choose a way of life. If the course is likely to be fifteen to twenty years it is mischievous to interfere very much with the patient's liberty to do what he wants, but if the end is likely in a year or two he would obviously be ill advised to embark on a new career or business venture in which illness and incapacity might bring great financial hardship.

Tests of renal function are of some assistance in this assessment. A maximum urinary specific gravity, after fluid restriction, of only 1010 to 1015 is bad, as is also a urea clearance of less than 40 to 50%. The symptom of nocturia usually, but not always, indicates termination within a year or two. A high diastolic pressure (120 or over) is incompatible with long survival, whereas a relatively low one (say 90 to 100) is favourable. A significant rise in blood urea indicates the approach of the terminal stage.

Prognosis in Type 2 Nephritis

The overall prognosis of Type 2 nephritis, as already stated, is unfavourable. In most cases oedema can be overcome, but gross albuminuria remains and hypertension with renal failure eventually ensue. By far the most accurate guide to prognosis is again the blood pressure. I have never seen recovery in any of my cases in which the blood pressure rose, whether early or late in the disease. If, on the other hand, it stays consistently normal despite oedema and heavy albuminuria complete recovery is always possible, and occurs in perhaps 20 to 30% of these normotensive cases. Some recover completely after several years of varying and recurrent oedema. A raised blood urea augurs a bad prognosis with as much certainty as a raised blood pressure.

Treatment of Type 1 Nephritis

Although our ability to treat nephritis is limited and our knowledge is incomplete, it is impossible even to make a logical attack on the symptoms without having some concept of the disordered physiology and biochemical changes of nephritis.

In acute nephritis the oedema seems to be due to salt and water retention. Whether this is in turn due to altered renal haemodynamics is not quite clear. The water retention gives rise to haemodilution, and the total body water is increased. These are the conditions which are probably responsible for causing convulsions, heart failure, and pulmonary oedema, all of which are complications to be avoided. When anuria or severe oliguria occurs it is not because the body lacks fluid, but because the kidney is not responding to the normal stimuli regulating fluid excretion. To give copious fluids in acute nephritis is therefore like giving sea-water to a drowning man. He has already quite enough.

All cases should be kept in bed throughout the acute stage. Fluid intake should be limited to 500–600 ml. until oedema is subsiding and diuresis established—that is, usually for a week or two. Salt should not be given. Calories should be provided in the form of carbohydrate and fat. Bread, butter, jam, biscuits, fruit, and sugar make up the diet at this stage. Milk is unsuitable, since it contains too much fluid, salt, and protein. When a favourable turn in the symptoms has occurred a light diet containing not much salt or protein is normally prescribed for a week or more before returning to normal food.

If an active infection such as tonsillitis is still present penicillin should, of course, be given, but it does not seem to influence the course of the nephritis, neither do the antihistamine drugs. Cases of acute nephritis, with wet lungs (pulmonary oedema) are very prone to secondary infection, which again requires penicillin. In rare cases in which total anuria occurs it may be treated by the conservative method now used in acute tubular necrosis. The object is to give the patient calories without protein or electrolytes. The method is described in Dr. D. A. K. Black's article (*British Medical Journal*, 1950, 1, 893) under "acute renal failure."

When a patient with acute nephritis has recovered he no longer requires treatment or burdensome restrictions on his

freedom, a fact insufficiently grasped by many doctors. Even in the latent stage it is doubtful whether dietary restriction influences the course of the disease, and it is usually better to let the patient do as he pleases.

The treatment of uraemia—that is, the terminal phase—has already been described in this series (*British Medical Journal*, 1950, **1**, 893).

Treatment of Type 2 Nephritis

Except in those rare cases mentioned in Part I of this article which appear to be due to calomel or troxidone, there is no such thing as curative treatment of Type 2 nephritis. All we can do is to make an attack on the oedema, which, after all, is usually the only symptom that troubles the patient, at any rate until the last stages of his disease.

The sequence of events in the formation of oedema in Type 2 nephritis appears to be as follows: heavy albuminuria causes loss of plasma albumin (hypoalbuminaemia). The normal transudation of fluid from capillaries to interstitial fluid is usually limited by the osmotic pressure of the plasma proteins. In hypoalbuminaemia this osmotic pressure is low and excess of fluid escapes, giving rise to oedema. The loss of fluid from the plasma causes a tendency to haemoconcentration, with a fall in blood volume, and to this the normal response of the kidney is to retain salt and water to build up the blood volume. Thus a vicious circle sets in, the kidney retaining more saline fluid to "replace" that which is lost from the plasma in oedema.

This vicious circle we can attempt to influence at various points. Obviously the right thing would be to stop the albuminuria, but this we have no means of doing. We can, however, give a high-protein diet, with a view to helping the body to replace its protein loss. This can be supplemented by hydrolysed protein foods. In addition we can restrict salt intake and give intravenous protein or other substances of high molecular weight.

For practical purposes a high-protein/low-salt diet is prescribed in the first place. If this is insufficient to keep the patient oedema-free we may be more strict and insist on salt-free bread, and supplement the protein with hydrolysates. If this still does not suffice, intravenous dextran (a high-molecular-weight carbohydrate solution) or intravenous human serum albumin may be tried if available. Intravenous concentrated human plasma is not advised for various reasons. It must be remembered, however, that, while such measures sound very logical, the patients are often losing from 10 to 20 g. of protein a day in the urine—that is, as much as is normally contained in two to three litres of plasma. Intravenous medication, therefore, needs to be on a grand scale if used at all.

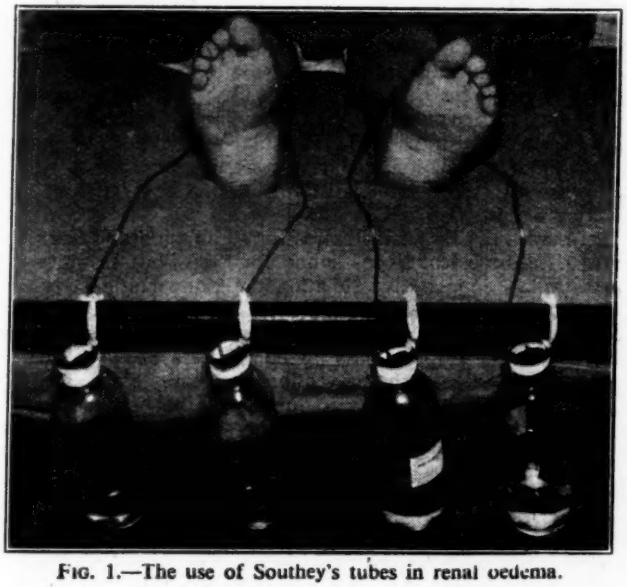


FIG. 1.—The use of Southey's tubes in renal oedema.

Fortunately, simple mechanical means of removing oedema are often very successful, and, once free from the major load, the patient may be able to keep his oedema in check by dietary measures alone. In grossly oedematous patients paracentesis of the chest and abdomen may be required. In addition the use of Southey's tubes, now that we have antibiotics to overcome infection, is often most successful. The patient is prepared by being kept propped up in bed for several days, with the legs as low as possible to drain the oedema into the dependent parts. While still in this position, two Southey's tubes are inserted into each leg, and the fluid is drained off into suitable receptacles through fine rubber tubes (Fig. 1). Southey's tubes can be kept in position for three to five days. In this way many litres of fluid may be removed, enormously increasing the comfort and morale of the patient (Fig. 2). It is interesting that fluid disappears not only from the legs but from the whole body, including the face, if the tilted posture of the patient is properly maintained.

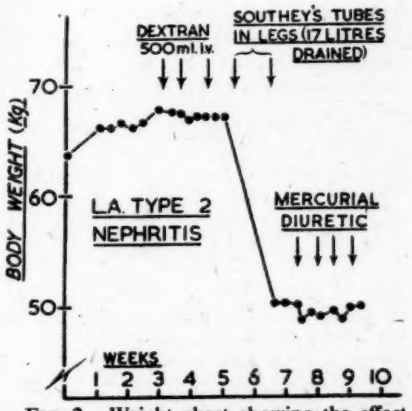


FIG. 2.—Weight chart showing the effect of draining oedema by Southey's tubes together with the relative lack of effect (in this case) of dextran and a mercurial diuretic.

Mercurial diuretics have a small but sometimes useful part to play in Type 2 nephritis. They apparently do no harm, but are not very effective, causing usually only a slight diuresis and minimal salt loss, not comparable with their dramatic effect in cardiac oedema.

So much for the accepted forms of treatment. In recent years other means of therapy have been tried. It has been known for a long time that oedematous nephritis is apt to undergo unpredictable spontaneous changes which may sometimes unexpectedly lead to complete remission or apparent recovery. Sometimes this has occurred after infections. In children with nephrosis the effect of infection by malaria has been tried, since it is relatively harmless and controllable, with remission or recovery in some cases. Nitrogen mustard has also been used and probably acts in a similarly non-specific manner.

A sodium depletion more efficient than that achieved by diet can be obtained by the use of ion-exchange resins, but these require careful control and are not yet suitable for use outside hospital. Finally, the effect of A.C.T.H. and cortisone has, of course, been tried. It can be said with some assurance that these agents do not seem to influence the disease fundamentally. During their administration sodium retention generally occurs and oedema increases. On withdrawal, however, a diuresis often takes place which may be followed by a prolonged remission in some instances, even with disappearance of proteinuria.

The treatment of renal oedema may be compared with that of cardiac oedema. By one method or another it is usually possible to keep the patient dry, and by so doing we add greatly to his comfort. It is rarely that we can honestly claim to have influenced the underlying disease.

Next Refresher Course Article.—"Disseminated Sclerosis," by Dr. J. W. Aldren Turner.

AUSTRALASIAN MEDICAL CONGRESS

[FROM A CORRESPONDENT IN AUSTRALIA]

The eighth session of the Australasian Medical Congress (British Medical Association) was held in Melbourne from August 22 to 29, under the presidency of Sir JOHN NEWMAN-MORRIS, a former chairman of the British Medical Association in Australia and deputy chancellor of Melbourne University. Melbourne was chosen as the meeting-place in honour of the centenary of the Medical Society of Victoria. This city, where the home Association held its 103rd annual meeting in 1935, is well suited to the holding of a congress. The University was in vacation and its several departments were made available to the congress, the headquarters being situated in the School of Anatomy. Associated with the congress were a comprehensive trades exhibition, a pathological museum, and an exhibition of doctors' hobbies.

Governor-General's Address

The opening ceremony was performed by the Governor-General of Australia, Sir William McKell, in the presence of nearly 3,000 delegates, the parent body of the Association being represented officially by Professor Lambert Rogers, of Cardiff.

In his opening remarks Sir WILLIAM MCKELL said that the occasion combined all the activity of a congress widely representative of medical science with the centenary of Australia's oldest medical society, the Medical Society of Victoria. He referred briefly to the early days of the Society, to the preservation of its identity even after its fusion with the Victoria Branch of the British Medical Association in 1907, and to the present high standard of medical practice, teaching, and research in Melbourne. Turning to the subject of the congress, Sir William suggested that the main incentive to attendance at such gatherings was the stimulating experience of meeting fellow members of the profession, including the especially able and eminent. He then spoke of the first medical congress in Australia, which described itself as "inter-colonial," and of the series of congresses up to and since they had been taken over by the British Medical Association in Australia.

Sir William McKell said that he had emphasized the value of the congress in its informal and social aspects, but naturally its contribution to medical knowledge was made chiefly through the papers read. He cited important pioneer work on the sympathetic nervous system presented at the congress in 1923, work which had played an important part in the development of surgery of that system, and suggested that presentation of work at a congress helped to gain it a wider and more appreciative world audience. He also referred briefly to Australian contributions to medical knowledge, including early work on filariasis and the transmission of disease by mosquitoes, the relationship of maternal rubella to congenital defects, the recognition of pink disease, the study of hydatid disease, the development of thyroid surgery, and the study of tropical diseases and "Q" fever. Sir William concluded with some remarks on the progress of medical thought and its present emphasis on positive health.

Rise of Medicine in Australia

Sir JOHN NEWMAN-MORRIS began his presidential address by thanking the Governor-General for his presence at the congress and asking him to convey a message of devotion and loyalty to the Queen, the Patron of the British Medical Association, of which the Australian Branches formed an important part. The president then reminded those present at the congress that advantage was being taken of this session to celebrate the centenary of the stabilization of medical organization in the State of Victoria and indeed in Australia. In the State of Victoria in 1839 there had been only six doctors to care for a population of 6,000. Among the six was David Wilkie, who might be regarded as the founder of medical organization. When the Port Phillip Medical Association was formed in 1846, 16 doctors had joined that infant body. This small body had kept together until 1851. It was in May, 1852, that Wilkie had revived the then scattered profession to form the Victorian Medical Association, out of which had grown the Medical Society of Victoria. Wilkie had been the first president, and the meetings for the first year or so had been held in his home. Wilkie had played an active part in establishing in 1856 *The Australian Medical Journal*, and among other things he had been responsible for the Bill establishing the *British Pharmacopoeia* as the legal basis for prescribing. Great credit was due to the young founders of the Society for their devotion to medicine in spite of the turbulent conditions which had surrounded them. At the present time in 1952 Australia was concerned with the difficulty of coping with an influx of migrants, but those difficulties appeared to be considerably less than those which had faced the Colony of Victoria in 1852, the year after the discovery of gold. In that year the population of Victoria had suddenly grown from 97,000 to 165,000. The young medical society had soon come upon troublous times. Sir John Newman-Morris quoted from an address by Richard Tracy in 1861, in which it was said that dissensions had taken place, that apathy was displayed, and that resignations had been received. Despite these, however, the loyal few had continued to hold the fort and had exerted considerable influence on the Government and on the community. There was no doubt that a small body of earnest doctors of those days had been responsible for much of the early medical legislation of the colonies. It was true that attention was often drawn to the lack of sanitary measures of the early days, but the president pointed out that the first public health legislation in the Old Country had not been until 1868. *The Australian Medical Journal* had had a continuous existence for 58 years until it was merged into the present federated journal, *The Medical Journal of Australia*. Its founder, John Maund, had died in 1858. The president said that few medical men could have accomplished as much as he did and have laid down so many sound foundations in such a short professional life.

Need for New Medical Schools

Sir John Newman-Morris referred to the work of the Society and its journal, and to the part that they had played in the establishment of a School of Medicine in Melbourne. This had taken place in 1863. Medical teaching had been undertaken in Sydney in 1883, in Adelaide in 1885, and in Brisbane in 1936. The existing medical schools had not only to educate students from the six States, but had the duty to find room for overseas students from near-by countries. The time was overdue for the foundation of medical schools in Western Australia and Tasmania, and indeed, with the growth of population, the time was not far distant when provincial medical schools would have to be opened in the larger States.

In Australia they still looked for stimulation and learning from medical leaders of other countries, but in spite of Australia's comparative isolation the claim could be made that Australian medicine had reached its majority in the period of 100 years. The members of the medical profession had a heavy responsibility to continue to show the community the value of the prevention of disease and to alleviate suffering. The scientific programme of the present session of congress had been designed to pay regard to present and future health problems. Ninety years earlier *The Australian Medical Journal* had expressed the hope that the Medical Society of Victoria might one day grow out of its limited proportions and become an association practically identical with the profession in Victoria—"a union of the profession in some sort resembling the British Medical Association would be of high practical benefit to us." Sir John Newman-Morris thought that it could be said that the congress was the fulfilment of that early hope.

The Henry Simpson Newland Oration

When Sir Henry Newland resigned the office of president of the Federal Council of the British Medical Association in Australia, the Council decided to commemorate his long and valuable service to the medical profession and to the community by instituting an oration to be delivered at each

session of the Australasian Medical Congress. It also decided to award a Henry Simpson Newland prize in surgery for an essay on a surgical subject. The first Henry Simpson Newland Oration was delivered this year, in the presence of Sir Henry Newland, by Sir VICTOR HURLEY, who succeeded Sir Henry as president of the Federal Council.

Sir Victor Hurley reviewed his predecessor's work and laid special emphasis on his activities on behalf of the Federal Committee and of its successor the Federal Council. He then went on to discuss the changing state of hospitals in Australia. At the conclusion a vote of thanks was accorded to Sir Victor Hurley on the motion of Dr. A. J. Collins, the present president of the Federal Council.

After the oration, honorary degrees were conferred by the Chancellor of the University of Melbourne upon the following: Professor C. H. Best, of Canada; Professor W. E. Le Gros Clark, of England; Professor E. C. Dodds, of England; Mr. John Foster, of England; Dr. N. McA. Gregg, of New South Wales (in recognition of his work on maternal rubella and congenital abnormalities); Dr. F. Avery Jones, of England; Sir Henry Newland, of South Australia; Dr. A. B. Reese, of the United States of America; and Professor Lambert Rogers, of Wales.

Scientific Programme

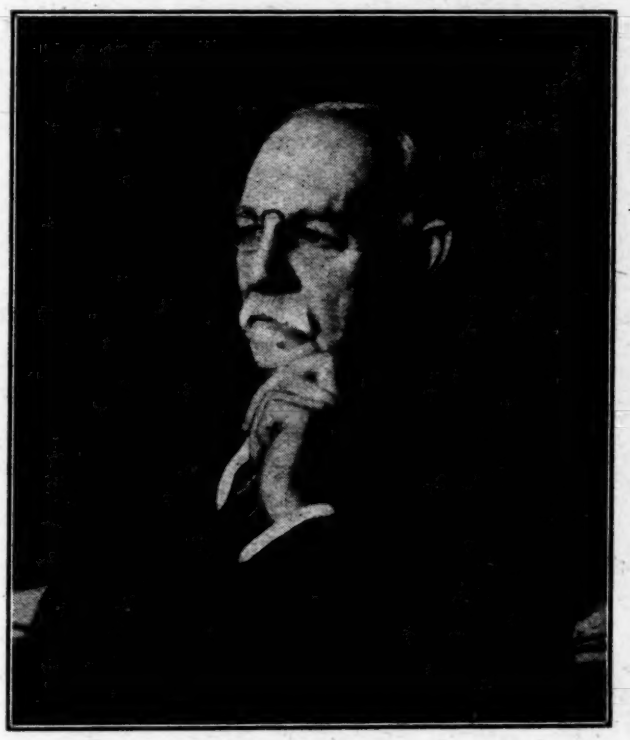
The scientific programme covered four days. Two days were given over to combined discussions. Two of these were panel discussions, which dealt respectively with hypertension and a review of the antibiotics. The subjects of the other combined discussions were: clinical problems of the menopause, a review of poliomyelitis, the uses of cortisone and A.C.T.H., recent advances in infectious diseases, mass management of burns, the medical care of the aged, the diagnosis and treatment of the common cough, and pruritus. The remainder of the work of the congress was carried out in Sections, which were: Anaesthesia; Dermatology; History of Medicine; Medicine; Naval, Military, and Air Force Medicine and Surgery; Neurology and Psychiatry; Obstetrics and Gynaecology; Ophthalmology; Orthopaedics and Physical Medicine; Oto-rhino-laryngology; Pathology, Bacteriology, Biochemistry, Experimental Medicine, and Forensic Medicine; Paediatrics; Public Health, Industrial Medicine, Tropical Medicine, and Aviation Medicine; Radiology and Radiotherapy; Surgery. Combined sessions of some of the Sections were arranged, and in each Section a presidential address was delivered by the president. Dr. F. Avery Jones and Sir Gordon Gordon-Taylor took part in a discussion on the management of the complications of peptic ulcer. Professor Le Gros Clark read a paper on the importance of the study of the "primitive" structure of the cerebrum. Mr. John Foster read papers on "the practitioner's guide to fundus oculi," "curiosa ophthalmica," the Budinger-Muller lid plastic operation, and the Ridley lenticulus operation. Dr. A. B. Reese (U.S.A.) discussed primary glaucoma, melanosis of the conjunctiva, and trends in cataract surgery, in three separate papers. Professor Lambert Rogers took part in a discussion on the thoracic syndrome. Symposia were held *inter alia* on the problems of epilepsy, and on the uses and abuses of sedative drugs, on prematurity, on Murray Valley encephalitis, and on the backward child. Dr. E. H. Derrick discussed the epidemiology of "Q" fever, and Dr. A. S. Walker described the history of the Australian hospital ships during the 1939–45 war. Dr. J. K. Maddox, of Sydney, described medical experiences in the surgery of mitral stenosis; Mr. F. H. Mills and Mr. C. J. O. Brown discussed the surgical aspects of mitral valve surgery.

Congress Dinner

The congress dinner was held on August 28, in the Exhibition Building, in the presence of Sir Dallas Brooks, Governor of Victoria, and Lady Brooks. The toast of the British Medical Association was proposed by Sir Owen Dixon, Chief Justice of the High Court of Australia. The reply was made by Dr. A. J. Collins, President of the Federal Council.

WILLIAM STEWART HALSTED

This year there have been celebrations in both America and Britain to commemorate the one hundredth anniversary of the birth of William Stewart Halsted, one of the great names among the founders of modern surgery. Halsted, whose ancestry was English on both sides, was born in New York on September 23, 1852. Elsewhere in this *Journal* (p. 655) the story of his life is told and his contributions to the science of surgery are recorded. Also in this issue the two volumes of Halsted's surgical papers, which were



specially reprinted for the centenary celebrations in Baltimore, are reviewed by Mr. David H. Patey (p. 653). The portrait on this page shows Halsted as he appeared towards the end of his life.

Appropriately the American centenary celebrations were held at Baltimore, for it was here, at the Johns Hopkins Medical School and Hospital, that the most fruitful years of Halsted's life were spent. On February 7 the Society of University Surgeons, the Society of Clinical Surgery, and the Halsted Club met there to honour Halsted. In the morning friends and pupils described the man they remembered; in the afternoon his work was the theme. It was as one of the afternoon papers that Mr. Patey, representing British surgeons, delivered his address on Halsted's influence on British surgery.

Britain honoured Halsted with a special meeting of the Section of Surgery of the Royal Society of Medicine, held on May 20. At this meeting Dr. Alfred Blalock, the present holder of the chair of surgery at the Johns Hopkins School of Medicine, gave an unforgettable account of Halsted's influence on surgery. Another surgeon from the Johns Hopkins Hospital and a former colleague of Halsted, Dr. S. J. Crowe, spoke of his personal recollections of Dr. Halsted. The British speakers were Mr. R. S. Handley, whose subject was the internal mammary lymph chain in carcinoma of the breast, and Dr. W. R. Bett.

At this meeting Dr. Blalock, who was accorded the honorary fellowship of the Royal Society of Medicine, presented a portrait of Halsted to Sir Cecil Wakeley for the Royal College of Surgeons, and Dr. Crowe gave Halsted's favourite walking-stick as a keepsake to the Royal Society of Medicine.

BRITISH ASSOCIATION

The one hundred and fourteenth annual meeting of the British Association was held in Belfast from September 3 to 10. It was attended by the Duke of Edinburgh as the Association's immediate past-president. For the second time since the war, the president was a physiologist, Professor A. V. Hill. Sir Henry Dale, also present at the meeting, was the first post-war president.

Professor A. V. HILL's address was on "The Ethical Dilemma of Science." He referred to the challenge of world-population, in relation not only to food but also such natural resources as power, chemicals, minerals, metals, water, and wood. A doubling of the survival rate (births minus deaths) in India during the last thirty years had led to a rate of population increase of 5 millions a year. Resolute measures to combat malaria and tuberculosis, and to improve rural and industrial health, would add a further one million a year to this figure. No one would dare to say that such steps should not be taken; but the consequences must be faced. There had been much discussion of human rights. At what level, he asked, could these be reasonably pitched? Did they extend to unlimited reproduction, with a consequent obligation falling on those more careful?

The section of physiology held a number of joint sessions with other sections. The biology of flying was discussed jointly with the engineers; the comparative physiology of muscle with the zoologists; antibiotics in animal nutrition with the agriculturists; and human biochemical genetics with the zoologists and psychologists.

The Biology of Flying

Dr. K. G. BERGIN (Medical Superintendent, London Airport) referred to the increasing use of air transport for invalids and sick persons, including those *in extremis*. There were practically no diseases or operative cases, including head injuries, which could not now be carried by air. The advent of pressurized cabins and the great reduction in vibration resulting from jet engines made transport in aircraft so equipped the method of least fatigue and discomfort. Diseases meriting special consideration, particularly with older-type aircraft, were those of the heart, blood, and lungs. Pregnant women, young children, and the aged travelled well by air, except in the worst possible weather.

Group Captain W. K. STEWART (R.A.F. Institute of Aviation Medicine) spoke on physiological factors which demand engineering solutions in military aircraft, and Mr. D. G. A. RENDEL on the same problem from the standpoint of physicist and engineer.

Comparative Physiology of Muscle

Flying as a natural activity entered also into the discussion on the comparative physiology of muscle introduced by Professor A. V. HILL (University College, London). He contrasted the case of the locust, in which the stored fuel, oxidative system, and oxygen supply must be adequate for an eight hours' flight at a rate of energy consumption 15 times as great (weight for weight) as that of an athletic man, with that of a humming-bird or bee, which works at a similarly high rate but can refuel at will. Whereas the wing muscles of the locust, during flight, rely entirely for energy on fat (lighter than any other possible fuel), the humming-bird or bee uses sugar almost entirely.

Dr. E. JEAN HANSON (Biophysics Research Unit, King's College, London) said that there was evidence for the migration of an unknown material, the "A substance," along vertebrate myofibrils during contraction induced by adenosine triphosphate.

Alimentation and its Disturbance

In his presidential address to the section of physiology, Professor R. C. GARRY (Glasgow University) reviewed the nervous control of movements of the alimentary canal. Presented as a companion description to that of humoral agencies given by Professor R. J. Brocklehurst at the 1950 meeting, the effect of this contribution was to underline the gaps and uncertainties in knowledge both of nervous outflow (particularly parasympathetic) to the gut and to nervous inflow from it.

Professor C. F. W. ILLINGWORTH (Glasgow University) summarized the results of an analysis of some 8,000 cases of perforated peptic ulcer recorded at a Glasgow hospital during the twenty years from 1924 to 1943, and discussed his findings in relation to other countries and continents. In Glasgow, the high wartime peak of 1940–1 coincided with the London peak, not with air-raids in Glasgow, and was accompanied by a similar acute rise in Scandinavia, including Sweden. The monthly incidence (low from mid-July to October, with a winter maximum in December), the weekly incidence (lowest, Sunday and Monday; highest, Friday and Saturday), and the diurnal incidence (high peak from 4 p.m. to 6 p.m.) all combined to suggest that high figures are related to periods of stress, and lower ones to rest or relief from strain—whether through the holiday season, the week-end, or a night's rest. Variations in geographical incidence suggested that differences in diet and possibly race were also relevant.

Nose and Ear

Dr. E. D. ADRIAN (Cambridge University) summarized recent research on the sense of smell. Recordings of nerve impulses from the olfactory organ suggested that odours are recognized from the total pattern of stimulation, in which there is great room for variety, rather than by specific receptors. The greater apparent sensitivity of many animals was to be attributed to better interpretation by their brains of the sensory information received, rather than to the possession of more sensitive receptor cells.

Dr. HALLOWELL DAVIS (Central Institute for the Deaf, St. Louis, U.S.A.) said that impulses in the auditory nerve could be initiated by disturbances of molecular and possibly even atomic dimensions. The amount of electrical energy dissipated in current-flow might greatly exceed the mechanical energy of disturbance. He suggested that the hair cells may provide a valve-like action by varying the electrical resistance of a specialized membrane in response to mechanical movement of the hairs.

The training of deaf children was discussed in the section of education. Professor A. W. G. EWING (Department of Education of the Deaf, Manchester University) said that in two weeks, with skilful training, a child aged 1 year had learnt to respond by specific acts of behaviour to six different phrases, distinguished by lip-reading. By the age of 2½ years a vocabulary of up to 500 words and phrases had been thus acquired. However, only about 1 in 20 of all children in schools for the deaf were found to be totally deaf, and with specially designed hearing-aids the majority of even severely deaf children could sufficiently distinguish speech-sounds to help them in lip-reading, linguistic development, and education.

Assessment of Intelligence and Personality

The assessment of intelligence and personality were discussed by the psychologists. Mr. A. YATES (National Foundation for Education Research) cited experiments to discover the effects of coaching and practice on intelligence-test scores. He concluded that the effect of coaching was negligible compared with that of the practice it involved, that the effects of coaching and practice were short-lived, and that there were marked variations in the response of groups of children given the same treatment. Professor P. E. VERNON (Institute of Education, London), in his presidential address to the section, said that, although quick and accurate methods of assessing personality appeared little nearer than 25 years ago, much of the spadework had been done, and it was merely a matter of time and hard work before a battery of relatively objective instruments was available.

Chemicals in Food

Professor W. WARDLAW, president of the section of chemistry, caused something of a stir at the meeting by his summary of the extent to which food adulteration is now legally permitted, and by his description of the extensive use of chemicals in food-processing. Under the latter head-

ing he listed preservatives, emulsifiers, colouring agents, flavouring materials, fat-extenders, "improvers," anti-staling and anti-acidity agents, sweetening agents, anti-oxidants, and antiseptics. Out of 704 extraneous substances said in evidence before the recent (U.S.) Delaney Committee to be added to food, there were 276 of which the safety was open to question, and "there is little doubt that the wide publicity which the subject is receiving will call for planned administrative action in Great Britain."

DEFERMENT OF RECRUITMENT FOR HOUSE OFFICERS

The Central Medical Recruitment Committee has decided that next year the practice of granting automatic deferment of recruitment to allow an "R" practitioner (that is, a doctor liable for National Service) to proceed from a second house officer post to a senior house officer post must be discontinued.

An "R" practitioner who completes six months in a second house officer post on or before December 31, 1952, will remain covered by the existing rules—that is, he will normally be allowed to take a senior house officer post for one year provided that it is secured before the end of his second house officer post, and commences within one month thereafter. An "R" practitioner who completes six months in a second house officer post on or after January 1, 1953, will require the special written permission of the Central Medical Recruitment Committee to proceed to any further post. The committee will not in any circumstances grant deferment to an "R" practitioner to hold any post during the tenure of which he will approach or pass his 30th birthday, the present age limit for the call-up of doctors under the National Service Acts.

There will be no change in the existing position in Scotland, where automatic deferment to proceed from a second house officer post to a senior house officer post was discontinued by the Scottish Central Medical War Committee in 1951.

Nova et Vetera

BLUFF KING HAL

Henry VIII: A Difficult Patient. By Sir Arthur S. MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S. Medical Viewpoint Series. (Pp. 202. 18s.) London: Christopher Johnson. 1952.

There can be no doubt that Henry VIII became a bloodthirsty monster, cruel, treacherous, vindictive, tyrannical. He did to death scores of innocent beings who were faithful to him and rejoiced in being so. But there can be as little doubt that to himself he did not appear the wicked man that he was. He was punctual and meticulous in his religious exercises, and there is every reason to believe that he regarded himself as a good Christian. The power of the human mind to deceive itself knows hardly any limits, and he was probably quite sincere when he wrote, not long before his death, "that he had been all his life a prince of honour and virtue, who never contravened his word." It is given to few of us to see ourselves as others see us, which is surely one excellent reason, among many, for humility in all of us. Yet such extreme discordance between the internal and external view of conduct as is apparent in Henry VIII can happen only to a madman or to an autocrat, for they, and they only, are insulated from all criticism. Sir Arthur's fascinating book is, in part, a study in the psychology of autocracy. But it is truly remarkable that cruel tyrants, such as Henry VIII or Hitler, can become and remain extremely popular with the very people they despoil. The book thus demands a companion volume on the psychology of this social phenomenon.

Much of Sir Arthur's book is devoted to the relationships of Henry to his ministers, combined with a general picture of the social life of the time. These are necessary for his two main themes, an investigation of the medical record of Henry and an account of his public relations with medical institutions and medical men.

It is commonly reported that Henry had syphilis. Sir Arthur effectively disposes of this. The medical record shows that, except for a severe attack of smallpox in 1514 and an occasional bout of malaria from 1521, Henry enjoyed superb health and vigour till 1528. In 1524, however, when jousting, he sustained a severe head injury with concussion, and thereafter was subject to headaches. These had become severe by 1527–8, when his character began to change. 1528 was the year of a serious outbreak of the sweating sickness. Thousands died in London, and the disease spread through the country. Anne Boleyn had a light attack. Her royal lover had previously shown personal courage, but now he carefully avoided her and fled from place to place as the disease spread wider. From now on Henry's mentality presents a contrast to that of his early life. Sir Arthur makes no attempt to explain his tyranny, heartlessness, and cruelty on medical grounds alone. There was evil deep-seated in the man. The French ambassador, Castillon, said of him: "I have to do with the most dangerous and cruel man in the world." Henry's maladies certainly helped to bring out the evil that a saner mental disposition would have controlled.

Henry had possessed considerable intellectual power. He had taken personal interest in medicine and accepted the guidance of certain medical humanists in securing some standard of medical competence. "With Sir Thomas More to advise him, Henry appeared to be interested in the welfare of his subjects and might have inaugurated public health and social reform on wise lines, for More had an outlook upon hygiene and public health which was greatly in advance of his time and in some respects in advance of our own time." More, an orator, a statesman, Speaker of the House of Commons, royal ambassador and Lord Chancellor, a master of English prose and a scholar, is renowned to-day as saint and martyr, for this gentle, highly civilized man was among the victims of Henry's abominable wickedness.

Henry's interest in medicine was fostered also by Thomas Linacre, to the lasting benefit of English physicians and perhaps to the welfare of the English public. The preamble of the Act of the third year of King Henry VIII recites that there were many ignorant persons, unlettered, common artificers, as smiths, weavers, and women, some being unable to read and yet professing to treat and cure disease, exercising "the science and cunning of physic and surgery, to the perfect knowledge whereof be requisite both great learning and ripe experience." The Act provided that no one should practise within the City of London or seven miles thereof unless he had been approved and admitted by the Bishop of London or the Dean of St. Paul's. In medicine the candidates were to be examined by four doctors of physic; for surgery by other expert persons in that faculty. Outside London and its precincts the examinations were to be conducted by the Bishop of the diocese, or his vicar-general, with such expert persons as might be convenient. The Act did not apply to medical graduates of Oxford and Cambridge, which had prescribed medical courses of their own, though of a purely literary character.

This reform, the first beginning of organization of the medical profession in England, was due to Linacre, who had seen in Italy the reputation to which the medical profession could attain. In the interests of the public health he wished to separate physicians and surgeons from the horde of empirics and quacks. He followed up this first essay by founding the College of Physicians of London in 1518. The Letters Patent stated that King Henry VIII was moved by the example of similar institutions in Italy and elsewhere, by the solicitations of his own physician, Linacre, and by the advice and recommendation of his Chancellor, Cardinal Wolsey. Sir Arthur has produced a charming and useful addition to the records of English medicine which provides a new outlook on a series of important events in the political history of this country.

CHARLES SINGER.

Correspondence

Anaesthetic Explosions

SIR,—The article on anaesthetic explosions by Dr. C. F. Hadfield (August 9, p. 332) is a very timely one. He rightly stresses the importance of having all potential sources of electric sparks as high above the floor as possible in order to prevent them coming into contact with heavy anaesthetic vapours. On a recent visit to Finland, I witnessed a rather frightening demonstration of this principle. At one of the larger hospitals I was invited into the theatre, where a gastrectomy was being performed under open ether given by a nurse. The diathermy needle was being freely used within two feet of the mask, the only protection being a mackintosh sheet hung over the anaesthetic screen. On inquiry I was informed that about 2,000 operations under open ether were done each year, that diathermy was employed in the majority, that the hospital has been in being for 20 years—and that there had never been an explosion.

An examination of the recorded instances of explosion in this country shows that the majority occur at or about floor level. In this connexion there is a hazard which I have observed, and which I do not think has been previously mentioned—namely, the sudden bursting into flame of the electric cable used to convey current to a movable operating light. When these lights, which are very heavy, are manœuvred about the floor of the theatre, quite often the cable is run over by the wheels. This causes damage to the insulation and an eventual short circuit. If these lights could be supplied by a cable hung from the ceiling, the theatre staff would not be able to trip over it and it would be a great deal safer.—I am, etc.,

London, W.1. MASSEY DAWKINS.

Death Following Fractured Clavicle

SIR,—The recent reports[1] of a man's death following fracture of the clavicle have drawn attention to this rare sequel of a common injury. It may not be generally known that the famous Sir Robert Peel (1788–1850) met his death from such an injury after a fall from his horse. He sustained a comminuted fracture of the left clavicle, and, though no operation was possible and no necropsy permitted, one cannot doubt the accuracy in diagnosis, or fail to follow the description of such a master of clinical surgery as Sir Benjamin Brodie, who attended him. Associated with Brodie were Caesar Hawkins and other eminent men. The following quotation from Holmes's life of Brodie[2] is in Sir Benjamin's own words, and forms part of a statement sent by him to Sir Robert Peel's executors.

"On the following day (June 30, 1850) there was no material improvement. The enlargement below the clavicle had increased, forming a swelling which could barely be covered with the hand. After some time it was observed that the swelling not only pulsated synchronously with the action of the heart, but (when examined carefully by the eye) that there was another movement perceptible in it, which seemed to correspond to the contractions of the auricle of the heart, resembling what may be seen in the veins of the neck in some very thin persons. From these circumstances there was sufficient reason to believe that there was a communication between the extravasated blood which caused the swelling and some large vein, and that the haemorrhage itself was the consequence of the subclavian vein having been lacerated by the splinters of the fractured bone, the pulsation being caused by the contiguity of the heart on one side and of the subclavian and axillary artery on the other. From the size of the swelling it was plain that the effusion of blood was very extensive, and sufficient to explain the faintness and collapse which immediately followed the accident and from which there was never anything more than a partial recovery afterwards. The extent of this effusion also explained (by the pressure which it made on the large nerves in the armpit) the exceeding pain which existed in the immediate neighbourhood of the injury as well as two other symptoms which were observed afterwards—namely, a sense of numbness and a partially paralytic state of the muscles of the hand and forearm.

"The state of prostration was such that at no period was it possible to venture on any considerable abstraction of blood. On one occasion, when there was some improvement in the state of the circulation, fifteen leeches were applied in the neighbourhood of the shoulder, but even the moderate loss of blood which these occasioned was followed by such a degree of exhaustion as made it necessary to administer wine and other stimulants.

"On July 1, in addition to the other symptoms, there was a violent and frequent cough, and the pulse, which on the previous day had been only 80, rose to 90 and then to 100 in a minute. With a view to arrest inflammation, and as the only means of doing so, an active mercurial treatment was begun and persevered in as long as there seemed to be any probability of its being useful.

"In the early part of Tuesday, July 2 (the third day from that of the accident), there was some apparent improvement, but it was only for a short time, and on the evening of that day Sir Robert Peel gradually sunk and died at eleven o'clock.

"It was ascertained after death that there had been a fracture of one or more ribs underneath the left scapula. By desire of the family no examination of the body was made after death."

A second case is recorded by Holmes.

"A few years after this event, a boy was brought into St. George's Hospital, dead, having been struck on the shoulder by a branch torn off a tree in Hyde Park in a storm. The clavicle had been fractured and a fragment had lacerated the internal jugular vein close to its junction with the subclavian. Mr. Caesar Hawkins was struck with the similarity of the injury to that which proved fatal to Sir Robert Peel."

The *Lancet* commented[3] shortly after Peel's death on the extreme difficulty of treatment.—I am, etc.,

London, N.7. JOHN W. DICKSON.

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1 *Daily Telegraph*, September 2.
2 Holmes, Timothy (1898). *Sir Benjamin Collins Brodie*. T. Fisher Unwin, London.
3 *Lancet*, 1850, 2, 19.

Prolonged Stupor and Anoxic Anaesthesia

SIR,—Dr. P. H. Mitchell (September 6, p. 535) gave a clear and detailed account of stupor coming on in a man 48 years old a few days after a surgical operation. This illness lasted for years and resulted in the patient being certified insane. In discussing the aetiology, Dr. Mitchell stated, "This hypothesis would almost demand an organic cortical inhibition. . . . In this connexion, it would have been helpful to be able to relate the anaesthetic given the patient at the time of his operation to the beginning of the psychosis, but there was a period of four days after the operation in which the patient appeared normal." Dr. Mitchell, therefore, though he suggested an organic lesion, dismissed anaesthesia as a possible cause on account of there being a lucid interval before the onset of psychotic illness.

On p. 533 of the very same issue of the *Journal*, Dark *et al.*, writing on "Acute Circulatory Failure During Surgical Operations," described (Case 2) the case of a woman admitted to hospital in the last stages of asphyxia due to haemorrhage into a thyroid cyst. They stated that, when the asphyxia had been relieved by intratracheal intubation and its cause removed surgically, and after the tube had been taken out, "the patient was actually able to thank the surgeon for saving her life, but she went into coma some 12 hours later and died within two days. At necropsy there were found to be multiple petechial haemorrhages throughout the brain. The appearances were characteristic of those seen in patients who have undergone long periods of asphyxia. It is of interest to recall that in certain cases of carbon monoxide poisoning there may also be temporary recovery of consciousness followed by coma and death, with similar post-mortem appearances." On p 535 (Case 8) these authors described a further case, this time of prolonged psychotic illness resulting from anoxic anoxia during anaesthesia. Sixteen months after operation this patient was still euphoric, having great trouble in learning shorthand, and "is probably going to show some slight permanent intellectual impairment, but not enough to prevent him earning his living."

Courville[1] stated: "While the literature is almost entirely silent on psychosis after nitrous-oxide–oxygen anaesthesia, no doubt if the effects were known a goodly number of these unfortunate individuals would be found in the insane asylums of this and other countries." And, speaking of transitory mental and emotional manifestations, he said[2]: "These patients go through an anoxaemic episode, present dramatic and alarming symptoms

shortly thereafter, but recover more or less promptly, apparently little the worse for the experience. It is very likely that if the facts were known such cases would prove to be more common than is now realized. Doubtless, the anaesthetist is glad enough to see the patient safely through the episode, and the story goes unrecorded." In a paper by Betten and Courville,[3] these writers stated their belief "that mental disturbances may occur more frequently after nitrous oxide anaesthesia than has been generally supposed." "It is likely," they said, "that cerebral and lenticular damage are due to the accompanying asphyxia (anoxic anoxaemia) and not to the toxic effects of nitrous oxide itself."

From these considerations and from the fact that Dr. Mitchell's patient, up to the age of 48, had been free from psychological illness, it seems more than likely that the condition which developed soon after his operation for hydrocele was the result of a severe or prolonged anoxic episode during anaesthesia. It would be valuable if Dr. Mitchell could furnish your readers with details of this anaesthetic and if he could state especially whether the hydrocele was tapped under the customary "whiff of gas." —I am, etc.,

London, S.E.1. J. G. BOURNE.

REFERENCES

1 *Untoward Effects of Nitrous Oxide Anesthesia*, 1939, p. 80. Mountain Ash, California.
2 Ibid., p. 87.
3 *Anesthesiology*, 1940, 1, 261.

Medical Education

SIR,—In your issue of August 30 there are nine articles on various aspects of medical education in this country and the U.S.A. Dr. A. M. Jones (p. 466) has especially interesting and constructive views. However, one aspect of this subject is neglected in the issue referred to. No mention is made of the teacher.

The component parts of a teaching unit may be said to be the teacher, the pupil, and the subject which is to be put to the one by the other in an intelligible manner. The qualifications for becoming a pupil are fairly satisfactorily laid down. The choice of subjects comprising curricula are frequently discussed; also the amount of time that should be employed on each subject, how the emphasis should be placed, and how subjects may be best integrated. In the sphere of teaching methods we consider how many beds should be allocated to each student, whether we should have more clinico-pathological conferences, and entertain thoughts for the future of televised bacteria. But how about our neglected medical teacher? Is he so expert at his job that his contribution goes without saying, or is he so bad that one cannot begin to discuss him? To be fair, the answer lies between those two extremes, but his qualifications are still ignored.

One knows of no medical school appointment where the selection was made on teaching ability. Without inside knowledge of how senior appointments are made—one can only judge by results—perhaps it would be fairer to say that many are made in spite of the candidate's lack of teaching qualities. Junior appointments are certainly made without reference to teaching ability. Has it ever been known, in the case of a job involving the teaching of clinical medicine, for a candidate to have been asked to take a group of junior students on, for example, the clinical examination of the cardiovascular system, to help the selectors decide his merit? I suggest, then, that teaching ability be given a place of importance in making medical school appointments, and dare to add that university teachers in general might benefit from a teaching course somewhat similar to that required for school-teaching.

May I close with two brief references to my own undergraduate career in a medical school where systematic teaching is compulsory and highly organized? On one occasion only did my class see the professor of an important basic subject—at the introductory lecture to the course. So much for his interest in teaching. Secondly, most people who have sat literally scores of examinations become able to gauge roughly the standard of their work each time. Having failed a non-professional "class examination," somewhat unexpectedly I approached the appropriate lecturer to ask after the manner of my downfall. I was told that discussion of such matters was completely against the rules, and that in any case the examination papers had been gone over thoroughly and there was no possibility of errors in correction. Is it not fantastic that students of this school are subjected to masses of termly examinations without being permitted to learn their mistakes, and to learn from them? —I am, etc.,

Arbroath, Angus. W. C. SHEPHERD.

General Practitioners and Postgraduate Education

SIR,—The recent educational number of the *Journal* (August 30) revealed all too clearly how little postgraduate education of general practitioners takes place in this country. There may be many reasons why relatively little use is made of existing facilities, but two are clear. First, the difficulty of leaving a practice in the hands of a stranger in order to snatch a much-needed holiday is great enough, but to prolong the period in order to attend a course of doubtful value seems more than the end in view would justify. Second, practitioners are doubtful whether two weeks of concentrated revision, most of which could not be assimilated in the time, are really likely to help them. It may be wrong, but I am sure that this feeling is widespread.

The problem should be approached in a different way. A small constant stream of instruction is likely to be comprehended more readily than the flood which is released under the present system. To this end the proposed College of General Practice could make a great contribution in two ways: (*a*) by the establishment of regional faculties, each conducting its own programme and local affairs, and contributing to those of the central body, and (*b*) by establishing academic goals towards which practitioners can travel, and the attainment of which would mark them as the best of their kind. These goals can no longer be provided by the existing Colleges, but only by a new body with no other branch of medicine to foster. I suggest diplomas graded as follows: (1) The graduate who is considered suitable to enter general practice as a principal. (2) The principal with some years of experience who has advanced his knowledge relevant to general practice. (3) The exceptional practitioner, who has a wealth of experience, the respect of his G.P. and consultant colleagues, and has contributed by his work to the advancement of general practice.

Given such a ladder to climb, some would reach the top, and the patients, the profession, and they themselves would all benefit. Furthermore, we would have in our midst some acknowledged experts who could play their part in the regional faculties in educating their younger colleagues, together with those specialists and consultants who were willing to contribute their knowledge and wisdom towards such an objective.

These are just tentative suggestions to fill two needs in the life of the general practitioner to-day. No doubt others can improve upon them, with the result, I hope, that something will be done to carry them out.—I am, etc.,

Sheffield, 7. H. H. PILLING.

The Couvade

SIR,—In your interesting annotation on this subject (September 6, p. 555) you do not mention the fact that Marco Polo found the custom among the Chinese in the thirteenth century. This fact is repeated in Samuel Butler's *Hudibras*, where the widow tells Hudibras:

> "Chineses thus are said
> To lie-in in their ladies' stead."

Ignatius Donnelly in *Atlantis* stated that the custom extended from China to the Mississippi Valley, and he reasons that a practice so absurd could scarcely have originated separately in two continents. It is put forward as a proof of the existence of the lost continent of Atlantis. I wonder whether the voyage of the Kon Tiki has rendered this argument invalid.—I am, etc.

Dudley. L. H. G. MOORE.

Confused Nomenclature

SIR,—Mr. Denis Browne's letter (August 16, p. 390) must not pass without comment.

There is no confusion in nomenclature. My cases were examples of severe spasmodic deformity due, presumably, to malposition *in utero*. The application of 25 to 30 successive divided plaster casts and very careful supervision secured complete success in the first 9 to 12 months of life. Improvement was a very gradual process, as might be expected. These infants would have had a severe "club-foot" with untreatable bony deformity had they not been corrected continuously from birth onwards.

My late chief, Mr. Robert Milne, orthopaedic surgeon to the London Hospital, successfully corrected cases of scoliosis by the Abbott's jacket method, and as his house-surgeon I was privileged to assist him and to learn from him. The principle is the same in both instances. Structure is adapted to function—law of Julius Wolff.

I deplore the existing warfare between the specialist and the general practitioner, but the G.P. must be allowed freedom to think for himself and to act as his training and reason direct.—I am, etc.,

Jersey, C.I. H. GORDON OLIVER.

Treatment of Sterility

SIR,—I feel that Dr. S. Bender (August 23, p. 409) in his excellent survey of the end-results of the work of the Liverpool Fertility Clinic does less than justice to his work in one particular instance—namely, the effect of the waiting-list.

After adoption, I have recently seen two cases of sterility of at least five years followed within a month or two by first pregnancy, and I believe the operative factor to be the same as that promoting pregnancy in cases on the waiting-list. As Dr. Bender says, the burden of infertility is transferred from the couple to the medical attendant, and, as a result of this, tension is relaxed, each act of intercourse is no longer a grim purposive attempt to establish a pregnancy, and so the tubal spasm, which I believe to be an important factor in the infertility of many of these patients, is released and pregnancy follows. I would suggest, therefore, that one of the most useful methods of treatment to be undertaken by a fertility clinic is to place the patients on the waiting-list for investigation after an interval of at least six to eight weeks, during which time I believe an appreciable number of pregnancies will be established.—I am, etc.,

Worcester. J. A. CHALMERS.

Dangers of Intrathecal Penicillin

SIR,—We feel that your Medico-Legal Correspondent's report (August 30, p. 518) of what is believed to be the first "myodil" fatality in Britain should not be allowed to pass without comment. Of the clinical data provided, we are impressed by the fact that an hour after an intrathecal injection of 200,000 units of penicillin the patient passed into status epilepticus and died two hours later. This syndrome can be produced by excessive intrathecal penicillin injections, and only within the last few weeks two similar cases have occurred in near-by hospitals. The first, a girl of 8 presenting with meningeal signs, was given 200,000 units of penicillin intrathecally and passed into status epilepticus a few hours later, followed by a prolonged stupor. She eventually recovered consciousness, but now has a residual hemiplegia with associated mental and moral deterioration. The second case was in a woman aged about 35, who presented with a meningeal picture and to whom 100,000 units of penicillin was administered intrathecally at the diagnostic lumbar puncture. About two hours later she started to have convulsions, which were eventually controlled by intramuscular paraldehyde, but for the next 36 hours she was stuporous and exhibited marked cerebral irritation before gaining normal consciousness. There were no sequelae in this case.

With the less purified forms of penicillin originally available, the dangers of intrathecal administration were well recognized; however, with the advent of the purer preparations it would seem necessary once again to emphasize its potential dangers. The almost limitless amounts of penicillin that may be injected intramuscularly or even intravenously without hazard are misleading, and our students are perhaps not sufficiently warned that the usual intrathecal dose should not exceed 10,000 to 20,000 units. We might also point out to them that, unless a cloudy fluid is obtained at diagnostic lumbar puncture, there is no indication for intrathecal therapy, and, furthermore, most cases of meningococcal meningitis will respond simply to sulphonamides by mouth.—We are, etc.,

London, N.W.10. VINCENT EDMUNDS.
R. J. PORTER.

Diet and Stamina

SIR,—May I furnish a footnote to the letter of Dr. A. Lewis (August 23, p. 445)? He writes: "One subgroup of vegetarians—the vegans—contrary to the prognostications of the nutritionists, managed to survive without any first-class protein whatever." I suppose animal protein is meant. Vegans eat no milk products, no eggs, no honey, and, of course, no other animal foods. The movement as such has been in existence for less than 10 years, but most of its members were previously vegetarian. They number several score and mostly belong to the middle classes.

Last year I saw as patients two members of about seven years' standing, a man and a woman, both aged just over 50. Both complained of pain in back and limbs, and informed me that members were accustomed to describe "the vegan back." Both had suffered from sore mouth, and from a form of onychia with blackening of the finger-nails. Both were aware of progressive ill-health and of failure to concentrate. Both were anaemic, the man markedly so.

The man was very thin and extremely stiff in all spine movements. Skiagrams demonstrated the changes of ankylosing spondylitis. His mouth was typical of riboflavin deficiency. He was a little depressed. The woman looked well nourished though slightly pale. She had signs and symptoms of subacute degeneration of the cord, and early spine changes suggestive of ankylosing spondylitis. She was alarmed at her reduced capacity for mental work, but bright and alert. Blood investigation done at the Royal Infirmary, Edinburgh, showed an anomalous type of anaemia in both cases. Both improved on a vegetarian diet to which eggs, milk, and butter were added: both patients refused to compromise any further with their principles. Both also received injections of vitamin B_{12}. They left Edinburgh feeling much improved.

They informed me that there had been several sudden deaths among members of the vegan group during the previous year or so. They expressed their intention of trying to make up the missing elements in their diet, notably perhaps iron and riboflavin, from non-animal sources. But their story does, I am afraid, justify the prognostications of the nutritionists.—I am, etc.,

Edinburgh. A. GUTHRIE BADENOCH.

Treatment of Recurrent Furunculosis

SIR,—I believe that the use of staphylococcus toxoid immunization is of very great value in the treatment of this condition. There are many who appear to think that an autogenous staphylococcal vaccine should be used. My experience, however, confirms the view expressed in Topley and Wilson's *Principles of Bacteriology and Immunity*, third edition, 1946, vol. 2, p. 1506, which reads: "There seems to be fairly general agreement now that toxoid is of considerably more value than vaccines of whole staphylococci. Furunculosis and staphylococcal skin lesions appear to be particularly benefited by toxoid treatment."

Many forms of treatment fall into undeserved disrepute because they are used incorrectly, and I am sure that the use of staphylococcus toxoid is an example. The course of immunization should, if at all possible, be commenced when the boils are quiescent. It is essential to start with a very small dose—for example, 0.1 ml. of the "weak" staphylo-

coccus toxoid (Parke, Davis). It is essential that the patient should have *no* local or general reaction after each injection. Patients are often very sensitive to the toxoid, and one man who received (contrary to my advice) the dose advocated by the makers was ill for three days with a severe local and general reaction. The injections are given at intervals of four to seven days, and the dosage should be increased cautiously. If there is a reaction the next dose should not be greater than the last one and may have to be less. The manufacturers also supply a "strong" staphylococcus toxoid which is five times as strong as the "weak" variety, and this should be used later on in the course of immunization.

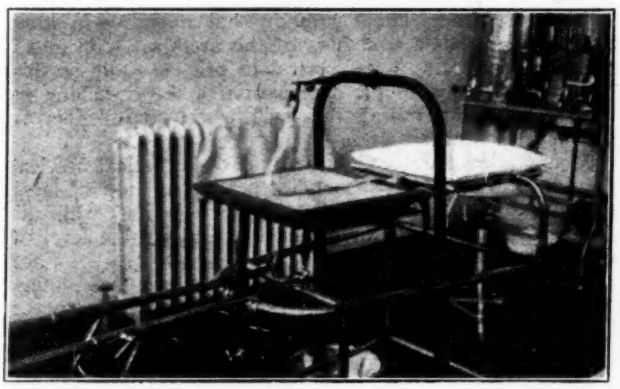
Other methods of treatment, such as swabbing the skin surrounding the lesions with 70% alcohol and the elimination of staphylococci in the nose by local application of penicillin or chloramphenicol cream, should not be neglected. Antibiotics given systematically do not, of course, prevent recurrence of the lesions.—I am, etc.,

Hull. J. G. ALEXANDER.

Adaptation of Watson-Jones Orthopaedic Table

SIR,—For a number of years I have been using a home-made adaptation to the Watson-Jones orthopaedic table for use in pinning the neck of the femur, and have found it so satisfactory that a brief description may be of interest.

The apparatus consists of the frame of an old *x*-ray screening-stand bearing a thin aluminium sheet, 16 × 13 in. (41 × 33 cm.), on which the patient's pelvis rests. Below this



frame is a tray to take the *x*-ray cassette, which can be worked from either side and most conveniently from the opposite side to the injury. The frame itself stands on three legs bolted on to the table, after the central pillar and pelvic rest of the table have been removed. The other part of the apparatus is a removable hoop, bearing a horizontal bar, which fits into sockets at either side of the table. This hoop is fitted into position when the patient is placed on the table, and incidentally acts as a convenient towel screen. At the extremity of the bar is a hook on to which a simple webbing strap is looped. The other end of the strap is attached to a central part of the table beneath the patient, while the strap takes the place of the usual perineal post.

The advantages of this arrangement are: (1) great ease in taking antero-posterior views; (2) perfect lateral views of the head and neck of the femur can be obtained, without any obstruction by a perineal post. The accompanying photograph should make clear the foregoing explanation.—I am, etc.,

Fermanagh County Hospital, Enniskillen. H. T. FLEMING.

Psychology and Psychiatry

SIR,—In company with Dr. Doris M. Odlum (August 16, p. 390) and other of your correspondents I find it discouraging that there are still acknowledged leaders in the profession who are unable to distinguish between a neurotic patient and a malingerer. On the other hand, the increased recognition given generally to the emotional factor in disease of all kinds is a source of satisfaction to those of us who in the past have felt that medicine is too materialistic. A recent number of the *Journal* (August 23) with its papers and discussion on "Mind and the Skin" is particularly notable, as, in addition, three out of the eleven answers to queries advise psychological assessment and treatment. I would like to ask where the unfortunate patient is to get the individual treatment required.

As far as my experience goes the average psychiatrist under the N.H.S. is so overwhelmed with cases that he sends even recently acquired anxiety states for shock treatment with scarcely any inquiries into their personal problems, and certainly without giving them insight. He will not welcome the addition to his list of chronic skins and grumbling appendices and everything else which may have a psychogenic factor.

Medical psychology has never been a popular specialty, and since it has become subsumed under the general title of psychiatry it is apt to be lost sight of altogether. The general practitioner who sends his neuroses to the psychiatrist gets little help now they no longer get any elucidation of their emotional difficulties and he tends to lose what faith he had. The patient, who always came to the psychologist as a last resort, is still more averse to seeking treatment now that he fears he may be lined up for "shock."

There are many psychologists who for one reason or another have not applied for psychiatric work under the N.H.S. Many of them have graduated into psychology the hard way through an interest stimulated by general practice and persevered with despite opposition. They have no *ad hoc* qualifications and little experience of the inside of a mental hospital, but they can apply their knowledge, and during the last two wars many did good service under the somewhat misleading title of neuropsychiatrists. Such men might be given the opportunity of forming psychology clinics as distinct from psychiatric clinics to deal with the class of patient I have been discussing. They could perhaps make little impression on the vast amount of material, but their work would help to educate the general practitioner so that more and more of them would learn how to deal with their own patients.

In my experience cases which require a long and deep analysis are rarer than they used to be and patients can be taught to make better adjustments to life in the course of a few sessions provided they are made to feel the object of a warm personal interest.—I am, etc.,

Scarborough. R. MACDONALD LADELL.

Hypnosis in Gynaecology and Obstetrics

SIR,—In Professor T. N. A. Jeffcoate's review of *Psychosomatic Gynecology*, by W. S. Kroger and J. C. Freed (September 6, p. 550), there is no mention of the use of hypnosis as a technique for obtaining "suggestive relaxation" in labour, or, in the form of hypno-analysis plus re-education of the patient, as an effective method of treating many functional gynaecological disorders. This omission seems rather singular, since the authors lay particular emphasis on this method of therapy, and cite numerous case histories where it was successfully employed for the above-mentioned purposes.

As this work demonstrates, there is now available a voluminous literature, drawn from world-wide sources, which describes the use of hypnotism in obstetrics and gynaecology, and I would have thought that more of our own practitioners of these specialties would have been interested in the subject.—I am, etc.,

London, E.18. G. F. NEWBOLD.

Tinted Glasses

SIR,—Samuel Pepys records in his diary how on returning home after a visit to one of his ladies he put on dark glasses "lest my wife should ask where I had been." Similarly to-day, when a patient, particularly a male, enters the surgery wearing tinted glasses, one can make a provisional diagnosis of "nerves." The blinkers will of course be hotly defended on the grounds of eye strain, or even that the specialist had "told me never to leave them off." But the impression of a

disturbed psyche remains and can often be confirmed by a glance at the footwear—for example, sandals retained in position by a complicated system of straps and buckles. In the case of women, this diagnostic point does not hold good, for women will submit to horn-rimmed spectacles of fantastic shape and size, in orange, yellow, green, and blue, simply because these monstrosities are displayed for gain in the shop windows, alongside photographs of film stars wearing them.

I do not suggest there is much of real harm in all this, but it does undoubtedly represent a form of *addiction* (the more one indulges, the more one has to). Moreover, it is, though perhaps unwittingly, a slur upon the Great Architect of the human eye, who made this organ so wonderfully flexible as to be able to cope with so great a variation in candle-power from wine cellar to the silver sea. I think it is perhaps the duty of the family doctor to explain the position to the patient, even at the slight risk of finding three months later a transfer to another doctor in the executive committee area; unless, of course, the doctor himself is wearing dark glasses too.—I am, etc.,

Buxted, Sussex. W. R. E. HARRISON.

Smokers' Cough

SIR,—For the last 30 years I have smoked an average of 20 cigarettes a day without any apparent ill effects, except a cigarette cough due to tracheitis. At the beginning of this year, for reasons of economy, I started making my own cigarettes with rice-paper. To my surprise, my cough vanished and has not returned. Two of my friends have had a similar experience.

Self-rolled cigarettes made with rice-paper do not remain alight when laid down as do most machine-made cigarettes, which leads to the inference that the latter have some addition to the paper (? saltpetre) to keep it burning. If this is the case, may not this addition have some bearing on the increased susceptibility of cigarette-smokers to carcinoma of the lung? The fact that pipe-smokers are not so affected would fit this theory.—I am, etc.,

Beccles, Suffolk. C. GRANTHAM-HILL.

Advertisements in the Post-bag

SIR,—May a medical bookseller be permitted to say a few words in reply to Dr. Desmond MacManus (August 30, p. 514) apropos the advertisements in his daily post? First, there is the story about the man who made the finest mousetraps in the world and wondered why nobody came to buy them. Surely Dr. MacManus does not wish to abolish medical advertising entirely, or would he prefer to see it concentrated in page after page of his professional journals? It would be a very dull world indeed if there were no advertising whatsoever. And what of the thousands of doctors living outside London, many miles from a large town, who are offered and can buy through the medium of the post the particular new drugs, equipment, and books which will keep them up to date? Regrettably there are, and probably always will be, certain firms who make exaggerated claims for their wares, but surely the answer in these cases is to make a request for one's name to be omitted from their mailing list.

Dr. MacManus asks two questions. The answer to the first one is that wartime controls on paper have been lifted, and, just as the size and value of this *Journal* have now been increased, so can the advertiser use more paper to promote the sale of, and give more information about, his products. To the second question, my reply is that a firm which spends most money in bringing its wares before the notice of the right people will reap the greatest benefit, always assuming of course it is a first-class article which is being offered for sale.

May I ask a question in turn? What induced Dr. MacManus to purchase the particular brand of cereal or marmalade which adorns his breakfast-table, or to buy that favourite brand of tobacco for his pipe?—I am, etc.,

London, W.1. DOUGLAS LUKE.

Acute Retention

SIR,—It appears to have escaped observation that the amphetamine–dextro-amphetamine sulphate group can be useful in the treatment of acute retention of urine in the male. I think that the urethral mucous membrane shares the decongestive effects of these vasoconstrictors noted in the nasal mucous membrane. I can quote two cases in which this treatment was successful. A male, aged 30, developed an over-distended bladder which he was unable to empty. Two tablets of amphetamine secured complete evacuation in 15 minutes. An elderly man with a hemiplegia and an enlarged prostate from time to time developed acute retention which again and again was relieved by amphetamine. A poor subject was thus spared operation or even catheterization. The amphetamine had the additional advantage of producing euphoria in a habitually melancholy individual.—I am, etc.,

Winchester. C. J. PENNY.

Urinary Retention and Pelvic Swellings

SIR,—We are all familiar with the clinical picture of acute urinary retention in association with the incarcerated retroverted gravid uterus. The absence of urinary symptoms with pelvic swellings which do not displace the cervix upwards is also a well-known fact. I was very impressed, therefore, when I was asked to see two patients in two successive weeks and both had had attacks of retention and in both there was a large uterine tumour but the external os was reasonably normal in position.

Reasoning from the assumption that retention in such cases results from a stretching of the urethra, I concluded that the tumour must be cervical in origin. Only in this way could I see a simple explanation of the stretching of the urethra from raising the level where the bladder is attached to the uterus.

At operation they both turned out to be typical cervical fibroids with small uterine bodies perched on top of large tumours about 5 in. (13 cm.) in diameter and with the uterine arteries coming in on each side above the level of the tumour.

I would therefore be very pleased to hear from other gynaecologists whether it is justifiable to conclude that a fibroid is a cervical one if retention occurs and the external os is in its normal place.—I am, etc.,

London, W.1 E. R. REES.

Essentials in Diseases of the Chest

SIR,—In an extremely fair and generous review of my book, *Essentials in Diseases of the Chest* (August 30, p. 478), Professor J. Crofton states that "it would surely be wise to mention the possible emergence of drug-resistant tubercle bacilli in patients treated with streptomycin, and the means of preventing this by giving P.A.S. simultaneously."

I feel that I should, in the interests of accuracy, point out that I did in fact refer to this important point, which may inadvertently have escaped his notice, both on page 145 and again in a special paragraph on streptomycin resistance on page 148.—I am, etc.,

London, W.1. PHILIP ELLMAN.

Farnborough Air Disaster

SIR,—On behalf of the director of the Royal Aircraft Establishment, the officer in charge of experimental flying, and the staff of the medical department of the Royal Aircraft Establishment, I would like, through the medium of your columns, to thank those doctors and medical students who gave their help during the tragic air disaster at Farnborough on September 6. It will be possible to give individual thanks to hospitals and medical staff, and this will be done in due course.—I am, etc.,

Royal Aircraft Establishment, South Farnborough, Hants. V. O. B. GARTSIDE.

Obituary

MARION GILCHRIST, M.B., C.M.

Dr. Marion Gilchrist, the first woman to graduate in medicine at a Scottish university, died at her home in Glasgow on September 7. She was 88 years of age.

Marion Gilchrist was born in Bothwell and educated at Hamilton Academy. After studying at home for a time and at Queen Margaret College, Glasgow, she started to attend medical classes in 1890, though it was not until two years later that the University allowed women medical students to sit its examinations. She graduated M.B., C.M. with high commendation in 1894. Though the first woman in Scotland to gain this degree, Dr. Gilchrist was not the first woman to qualify, for several had previously taken the Scottish triple qualification.

After leaving hospital Dr. Gilchrist spent some time as an assistant in general practice before setting up in practice on her own. She specialized in ophthalmology and was assistant ophthalmic surgeon at the Victoria Infirmary for 20 years, as well as being ophthalmic surgeon to the Redlands Hospital for Women. During the first world war she accepted a major share of the work of the ophthalmological department of the Infirmary. She published several papers on her specialty in this and other journals.

In her youth Dr. Gilchrist was a keen Liberal and a supporter of the suffragette movement. Later on she worked most actively for the Medical Women's Federation, being several times president of the West of Scotland Branch. She was also one of the trustees of the Muirhead Trust, which has helped many women to become doctors and medical research workers. Her interests extended far beyond her chosen profession. In spite of her academic record she was never the traditional "blue-stocking," but an attractive woman interested in all aspects of humanity, particularly music and art. Her friends were drawn from a very wide circle.

Dr. Gilchrist was a member of the B.M.A. for 54 years. In 1928 she was elected chairman of the old Glasgow North Western Division, and three years later chairman of the reconstituted Glasgow Division, which she represented at Annual Meetings from 1930 to 1937. She retired from active work about ten years ago.

C. E. TANGYE, C.B.E., M.D., D.P.H.

Dr. C. E. Tangye, formerly county medical officer of Wiltshire, died on August 20 at his home in St. Mawes. He was 74 years of age.

Claude Edward Tangye was the third son of Edward Tangye, who was one of a famous group of five brothers who founded a great engineering firm in Birmingham during the nineteenth century. He was educated at Blundell's School, and in childhood already showed a strong interest in doctoring and medicine. In spite of financial difficulties, and after a false start as a schoolmaster, he determinedly pursued his medical bent, graduating M.B., B.S. at Birmingham University in 1905. He then held resident appointments at the Queen's Hospital, Birmingham, and was resident medical officer at the old Birmingham Children's Hospital in Broad Street. After proceeding M.D. in 1907 (qualifying for the gold medal in medicine), he took the diploma in public health in 1909 and was then appointed medical officer of health to a number of local authorities in mid-Warwickshire.

In 1919 Tangye was appointed medical officer of health for Wiltshire. During his 26 years in the county he built up the public health service to a high standard of efficiency by his energy, power of organization, and broad outlook on the many questions affecting the health and well-being of the community. Soon after taking up work in Wiltshire he realized the need for a scheme for orthopaedic treatment and was instrumental in starting the first Wiltshire clinic in 1923. The scheme developed rapidly under his guidance, and with the help of the staff of the Bath and Wessex Children's Orthopaedic Hospital, until it became one of the most comprehensive for orthopaedic treatment in the country. Another outstanding feature of Tangye's administration was his interest in the co-ordination of the work of the public assistance department with that of the medical department. In 1933 he introduced, as an experiment, the "open-choice scheme," giving patients on medical outrelief free choice of doctor. This scheme proved entirely successful and gradually replaced the old arrangements.

In 1928 Tangye was appointed a member of the Departmental Committee on Maternal Mortality and Morbidity and was associated with the other members in the submission of both the interim and final reports. He was president of the Wiltshire Branch of the B.M.A. in 1927, and he served on a number of the Association's committees.

His services to public health were recognized after his retirement by the award of the C.B.E. in 1944.

Tangye had a pleasant sense of humour and great humanity under an apparently dry approach. He had a marked integrity of character and a determination which carried him through to an outstanding position in his chosen field of public service. His main interests in his spare time were the classics, and in particular the works of Homer, which he enjoyed until his last illness. Tangye married Eva B. Oakden in 1910, and never fully recovered from the blow dealt him by her death in 1948.

The death of Dr. S. B. MALIK occurred suddenly at Dar-es-Salaam on August 16. He was one of the longest-established private practitioners in Tanganyika, and played a notable part in public affairs there. Sultan Bakhsh Malik was born at Multan in the Punjab in 1899, and came to England to study medicine at Charing Cross Hospital shortly after the end of the first world war. After qualifying in 1925 he was for a short time in practice in Manchester, but in 1926 he took the D.T.M. at Liverpool and went out to Dar-es-Salaam, where he joined Dr. K. M. Rana in practice. From the first he showed a keen interest in local affairs, and his marked ability and untiring keenness in voluntary work of all sorts were maintained up to the day of his death. Not long after his arrival in Dar-es-Salaam he was nominated to the township authority, which he served for many years, being president for eight years. When the town attained municipal status he continued to serve as a councillor. He was nominated to serve on the Legislative Council for two periods, from 1930 to 1935 and again from 1939 to 1944. During his second period of service he was nominated a member of the Executive Council. In the second world war he served voluntarily as an assistant director of man-power and also as chairman of the Commodity Distribution Board. He was awarded the O.B.E. for his public services in 1943. Besides taking a prominent part in the activities of the local St. John Ambulance Brigade over many years (at the time of his death he was its president), he was also keenly interested in scouting, and was chairman of the local association. For many years he was a member of the Medical Registration Board of Tanganyika, and he was a keen and prominent member of the Tanganyika Branch of the British Medical Association, of which he was

president at the time of his death. Despite his multifarious activities he continued to conduct a busy practice. He was most successful in using his influence against the development of racialism and in breaking down the barriers between the various communities. Himself a Muslim, he retained a broad and open mind on all subjects, which, coupled to his infinite capacity for never losing his temper, earned him the respect and admiration of all classes and all creeds. In the best traditions of his profession his life was devoted to humanity, and on his death Tanganyika has lost a citizen who made a great contribution to the harmonious development of the country.

Dr. MURIEL KEYES, who had practised in Harrogate for 30 years, died at her home there on August 20. She was 67 years of age. Muriel Keyes was born at Chigwell, Essex, and studied medicine at Edinburgh and Leeds, qualifying in 1920. She held a number of resident appointments at the Leeds General Infirmary, and was later appointed honorary clinical assistant at the Hospital for Women in Leeds. In Harrogate she held an honorary appointment as gynaecologist to the Royal Bath Hospital and Rawson Convalescent Home. She published a number of papers on gynaecological subjects, and collaborated in writing the section on diseases of women in the book *Baths and Medical Waters of Great Britain and Europe*. Dr. Keyes was a keen horsewoman, and until the outbreak of the last war she hunted regularly with the York and Ainsty (North). Among her other interests singing had an important place, and she was a member of the Harrogate Madrigal Club for a long time. Dr. Keyes had a serious operation last November, and earlier this year she returned from convalescing in Switzerland. A memorial service was held in St. Peter's Church, Harrogate, on August 28.

Dr. GUY JOSEPH BRANSON died at his home in Edgbaston, Birmingham, on September 2. He was 82 years of age. Before taking up the study of medicine he took an arts degree at London University, and he then became a medical student at Queen's College, Birmingham. He qualified in 1894, graduated M.B. (London) in 1895, and proceeded M.D. in 1900. He practised in Birmingham all his professional life. His special interests were neurology and psychology, and at one time he was neurological consultant to the Ministry of Pensions.

Dr. James F. Brailsford writes: With the passing of Dr. Guy Branson, Birmingham citizens have lost one of their outstanding doctors, and his closer associates will mourn the loss of a loyal and stout friend. For nearly 60 years he exhibited the highest traditions of medicine to the great benefit of his patients and to the honour and glory of his profession. His brusque manner, his careful scrutiny of men and material, of patient and doctor, may not have brought him the recognition of a popular doctor, but his rigid integrity, his firm honesty of purpose, his searching inquiry into all things reported to be good for his patients, entitled him to the term wise physician. He was one of the old school of family doctors, and those who were fortunate enough to be his patients found in him always a true guide, philosopher, and friend. He respected academic status and position only when it was coupled with honest endeavour, but all who came into contact with him, be he patient or consultant, experienced a chastening discipline—a discipline which has done more to establish the high standard of British medicine than all the showy exponents of the "scientific" fashions of the time. Branson had a profound respect for, and knowledge of, psychology, which gave him a clear insight into human thought and conduct, and this, coupled with his wide reading and experience, his love of the truth, and sound appreciation of all modern advances, fitted him to assess values. He did not tolerate the shallow enthusiast, but he was kind and encouraging to all who showed an earnest desire to render honest service. He was opposed to the exploitation of medicine, be it private or public. The profession has been ennobled by his services, for he set a high pattern throughout a long and useful life.

Dr. NORMAN HAIRE, the president of the Sex Education Society and author of many works on birth control and sex education, died in London on September 11 aged 60. Norman Haire was born in Sydney, New South Wales, and educated at Forte Street Model School and Sydney University. After graduating M.B., Ch.M. in 1915 he held a number of resident posts in hospitals, including No. 4 Australian General Hospital and the Hospital for Sick Children in Brisbane, and served in the Australian Army Medical Corps. He came to this country in 1919, and immediately took an active part in spreading knowledge about birth control. In 1921 he helped to found the Walworth Welfare Centre, where contraceptive advice was given to the mothers who attended. The work of Steinach and Voronoff on rejuvenation was much discussed in the nineteen-twenties, and Haire made a special study of it. He was convinced that many of the ills of mankind were due to sexual maladjustment, and he wrote many papers and books on the subjects in which he was interested, including the *Encyclopaedia of Sexual Knowledge*, which was published in 1934. He travelled widely, and attended many international congresses as a delegate from England. In 1925 he was president of the contraceptive section of the Third International Birth Control Conference, held in London, and in 1929 he organized the Third International Congress of the World League for Sexual Reform, of which he was co-president. Dr. Haire was unmarried.

Dr. FELIX EMANUEL ROSENTHAL, formerly professor of medicine at the University of Breslau, died recently in his 68th year. He came to this country in 1938 as a victim of the Nazi regime, and settled in Leicester, where he spent the remainder of his working life. Originally an assistant in Morgenroth's serological department in the Pathological Institute of the Charité in Berlin, he continued at Breslau under the celebrated Minkowski for a further 12 years, eventually being called to the post of director of medicine at the Jewish Hospital in Hamburg. The abrupt change from a semi-academic life to general practice would have daunted most men of middle age, but Rosenthal continued his work in the department of experimental medicine at University College, Leicester, and threw himself into his new life with enthusiasm. He established himself at the same time in Leicester as a popular doctor, most highly regarded by his colleagues and patients alike. His publications included many papers on haematology, the reticulo-endothelial system, and the liver, on which he wrote an excellent book. The kindest of men, Rosenthal combined devotion to duty and scientific interest to an unusual degree. He was indeed a typical representative of all that was best in German medicine during the first three decades of this century, and the impressive attendance at his funeral is a measure of the affection and admiration felt for him in his adopted town.—A. L.

Medico-Legal

DEATH FROM NUPERCAINE POISONING

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On May 21, 1951, Miss Evelyn Ann Warner, aged 19, was admitted to Ashford Hospital, Middlesex, for treatment for pulmonary tuberculosis. On November 19, 1951, she was prepared for the operation of thoracoscopy, but this was not carried out, because she appeared rather shocked after an injection of about 10 ml. of 2% "novocain."

On November 24 she was tested for sensitivity to nupercaine with 2 ml. of 2/1.000 nupercaine, and as the test was negative the operation was planned for December 3, with nupercaine as the local anaesthetic. On November 26 the house-physician ordered 30 ml. of 2% nupercaine from the dispensary, intending that it should be diluted at the surgeon's discretion.

On December 3 before starting the operation the surgeon was told by the house-physician that 2 to 3 ml. of nupercaine had been injected into the patient as a test without local or general reaction, and took this to mean 2 to 3 ml. of the same strength as that contained in the bottle which accompanied the patient to the theatre and which was 2% nupercaine as ordered from the dispensary. Accordingly he used it without dilution, injecting in all 5 to 6 ml. About 20 minutes after the operation started the patient said she felt sick and retched. After a few more minutes the operation was discontinued. The patient's head was lowered and her face wiped with water. She said she felt better, and looked better. She was moved to the ante-room. In a few minutes she had a convulsion, shortly followed by another. In spite of treatment she died within half an hour.

Giving evidence at the inquest at Twickenham on December 13, 1951, Dr. Donald Teare, who performed the necropsy, said that the operation on the fairly dense adhesions in the lung was clearly necessary, and had been skilfully carried out, but he had no doubt that the concentration of 2% nupercaine proved too strong for the patient. He gave as the cause of death bilateral pulmonary tuberculosis accelerated by over-dosage of nupercaine.

A verdict of death by misadventure was accordingly recorded.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in the week ending September 6 (36th week of the year) were as follows: paralytic 115 (150), non-paralytic 73 (65); total 188 (215). This is a decrease of 27 compared with the previous week, the figures for which are in parentheses. Up to and including the week ending September 6 the overall uncorrected notification rate for England and Wales was 6.4 per 100,000.

Infectious Diseases

The only large fluctuation in the incidence of infectious diseases in England and Wales during the week ending August 30 was a decline of 1,607 in the notifications of measles. The next largest variation was an increase of 61 for whooping-cough.

The number of notifications of scarlet fever was 2 less than in the preceding week and there were no large local variations in the trends. The chief feature of the returns of whooping-cough was an increase of 51 in the number of notifications in Essex. The number of notifications of diphtheria was 1 less than in the preceding week; the largest centre of infection was Birmingham C.B. with 4 cases. The largest declines in the incidence of measles were Yorkshire West Riding 320, London 161, Lancashire 120, Surrey 116, Glamorganshire 113, and Essex 102.

The number of notifications of paratyphoid fever was 14 less and for typhoid fever 9 less than in the previous week. The largest returns for paratyphoid fever were Monmouthshire 9 (Pontypool U.D. 5), Glamorganshire 8 (Aberdare U.D. 4), and Durham 6 (Easington R.D. 5).

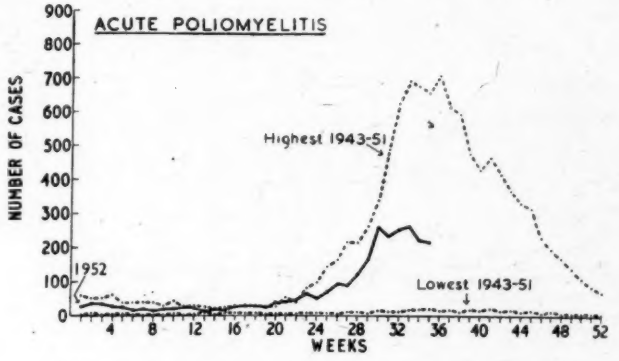
The notifications of acute poliomyelitis were 2 less for paralytic and 3 less for non-paralytic cases than in the preceding week. The chief feature of the returns was an increase of 16 in London and a decrease of 18 in Yorkshire West Riding. The largest returns during the week were London 27 (Islington 6), Essex 19 (Southend-on-Sea C.B. 4), Yorkshire West Riding 18, Middlesex 14 (Edmonton M.B. 4), Kent 11, Lancashire 11 (Liverpool C.B. 4), and Durham 10.

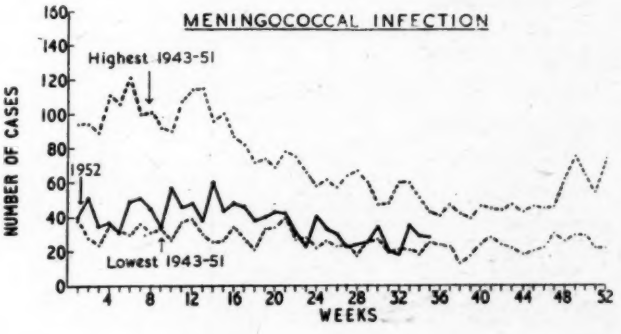
In Scotland 19 cases of acute poliomyelitis were notified, the largest weekly total during this year.

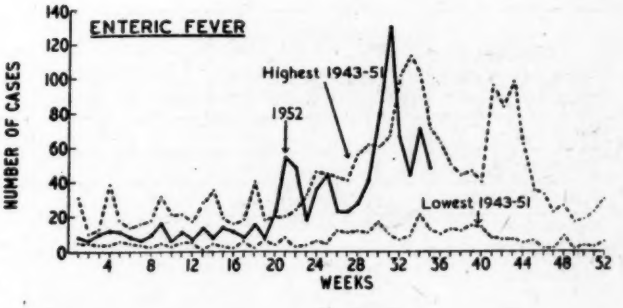
The number of notifications of dysentery, which was 29 less than in the preceding week, was the lowest for nearly three years. The largest returns were London 17 and Middlesex 10.

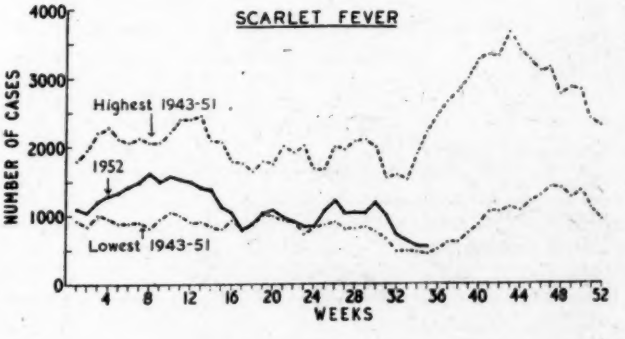
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1943–51 are shown thus - - - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending September 6

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 557, whooping-cough 1,831, diphtheria 23, measles 2,937, acute poliomyelitis 188, dysentery 132, paratyphoid fever 41, and typhoid fever 7.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 30** (No. 35) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng & Wales	Lond.	Scot.	N. Ire.	Eire	Eng & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	22	2	3	0		35	4	9	0	1
Dysentery	90	17	94	6	3	152	32	72	3	1
Encephalitis, acute	8	1	0	0		10	0	0	0	
Enteric fever:										
Typhoid	4	0	0	0	1	2	2	1	0	0
Paratyphoid	44	1	2(B)	1	2(B)	37	1	0	4	2(B)
Food-poisoning	139	20		0		123	12		3	
Infective enteritis or diarrhoea under 2 years				19	66				11	39
Measles*	3,649	412	42	56	108	1,876	68	67	77	40
Meningococcal infection	28	2	7	1		36	4	12	1	2
Ophthalmia neonatorum	28	6	11	0		31	4	11	0	
Pneumonia†	220	9	135	6	2	217	8	137	1	
Poliomyelitis, acute:										
Paralytic	150	15	19	9	1	35	3	7	1	
Non-paralytic	65	12				54	3			
Puerperal fever§	216	31	9	0		234	31	11	2	
Scarlet fever	557	49	151	14	46	461	29	108	16	19
Tuberculosis:										
Respiratory			151	19				143	32	
Non-respiratory			34	4				30	14	
Whooping-cough	1,861	83	107	41	105	2,727	107	297	62	78

DEATHS in Great Towns	1952					1951				
	Eng & Wales	Lond.	Scot.	N. Ire.	Eire	Eng & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0		0	0	*0*	0	*0*	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		1			0		0			1
Enteric fever	0	0		0		*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	7	0	1	0		*8*		*3*	1	0
Influenza	1	1		0		*3*	1	*0*	0	0
Measles		0		0	0		0	*0*	0	0
Meningococcal infection		1					0	*1*		
Pneumonia	129	21		5	3	*133*	14		11	5
Poliomyelitis, acute	9	0			0	*1*	0			0
Scarlet fever		0			0		0	*0*	0	0
Tuberculosis:										
Respiratory	87	6	11	2	2	*130*	8	*22*	1	8
Non-respiratory		4	3	0	0		3	*5*	0	2
Whooping-cough	1	0		0	0	*2*	0	*0*	0	0
Deaths 0–1 year	216	22	26	8	17	*181*	25	*30*	7	14
Deaths (excluding stillbirths)	4,268	620	475	90	118	*3,975*	621	*557*	100	148
LIVE BIRTHS	7,348	1141	757	208	352	*6,646*	1169	*756*	218	395
STILLBIRTHS	165	21	22			*183*	22	*21*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

International Congress of Internal Medicine.—The second International Congress of Internal Medicine—the first was held in Paris in 1950—was opened in London, at Friends House, on September 15 by Sir Russell Brain, P.R.C.P. He was accompanied on the platform by the Rt. Hon. Iain Macleod, M.P., Minister of Health; the Mayor of St. Pancras; Sir James Paterson Ross, Vice-President of the Royal College of Surgeons; Dame Hilda Lloyd, President of the Royal College of Obstetricians and Gynaecologists; Lord Moran, honorary vice-president of the Congress; Sir John Charles, Chief Medical Officer of the Ministry of Health; Dr. Roger Lee, past-president of the American College of Physicians; Dr. A. Gigon, president of the International Society of Internal Medicine; and Sir Harold Boldero and Dr. W. G. Barnard, respectively secretary and treasurer of the congress. In a brief address to the distinguished assembly, which included representatives of 29 countries, the Minister of Health said that it was an excellent thing, when there was so much specialization, to have a congress which brought back to their minds the fundamental importance of general principles. Dr. A. Gigon referred to the recent growth of national societies of internal medicine, a number of which had made their appearance since 1948. Internal medicine, he said, made for harmony, not only between the different branches of medicine but between medicine and the other sciences. Dr. Roger Lee said that internal medicine had no language of its own, and did not demand a particular tongue to give it expression. Science and the creative arts were the only disciplines which had a universal appeal and a universal language, and perhaps the applied science of medicine—in some respects an art—was paramount in such universal appeal. Sir Russell Brain, in welcoming the members to London, after reading a message from the Queen, the Patron of the congress, said that he had been often asked, "What is internal medicine?" What was the difference between this congress and congresses concerned with specialized subjects such as gastroenterology, biochemistry, bacteriology, and neurology? Internal medicine dealt with the whole man, but, after all, so did the specialties; but the specialty saw the whole man from its particular angle, whereas internal medicine saw all the aspects from the standpoint of the whole man. It was proper to place emphasis upon the comprehensive view, and that was the main function of the congress, which he then declared open.

Cardiologists' Banquet.—The official banquet of the First European Congress of Cardiology was held on September 12 at Grosvenor House with Sir John Parkinson, president of the British Cardiac Society, in the chair. After Sir John had proposed the toast of "The Guests," Mr. Iain Macleod, the Minister of Health, proposed the health of the European Society of Cardiology. Professor Gustav Nylin, president of the Society, and Professor Pierre Rylant replied. Subsequent speakers included Dr. Irving Wright and Professor Charles Laubry.

After Straffen.—Recent letters to *The Times* on the inadequacy of the M'Naghten rules have included several from eminent members of the medical profession. The president of the Royal College of Physicians, Sir Russell Brain, advocated a Royal Commission to look into the matter. Dr. Letitia Fairfield drew attention to the existing provisions of the law concerning mentally defective criminals. Sir Reginald Watson-Jones, a vice-president of the Royal College of Surgeons, while agreeing with Sir Russell Brain on the need for a Royal Commission, suggested that the Commission should "consider the advisability of abolishing hanging for those whose minds are normal, and arranging a peaceful and endless sleep for those who murder without knowing it." Dr. A. Piney discussed the diagnosis of insanity. Dr. T. Rowland

Hill reminded the public of the B.M.A.'s evidence to the Royal Commission on Capital Punishment, and drew attention particularly to the merits of the Scottish law of diminished responsibility. (It is understood that the report of the Royal Commission on Capital Punishment will be available before the end of the year.)

General Practice on Television.—The television programme "Family Doctor," which was broadcast on September 3, seems to have been generally enjoyed by the public and welcomed by most of the professional critics. This second documentary programme on a medical subject was written by Cormac Swan (assistant editor of the B.M.A.'s popular health magazine *Family Doctor*) and Robert Barr, who also produced it. The same team were responsible for the earlier and very successful documentary, "Dangerous Drugs." "Family Doctor" lacked some of the dramatic interest of the earlier programme, but it was none the less a workmanlike job, marked by its sincerity and authenticity: the whole script, from start to finish, was essentially based on facts. As entertainment "Family Doctor" sustained its interest throughout.

Copyright Convention Signed.—After a three-week conference at Geneva, called by Unesco, representatives of over 40 countries signed a new international copyright treaty on September 6. The treaty establishes a universal 25-year minimum copyright protection for both foreign and domestic authors. The United States was among the signatory countries, but not the Soviet Union or its satellites. Before the treaty comes into force it must be ratified by 12 countries, including the United States, where new legislation will be required.

Royal Society of Edinburgh.—New members of the Society elected this year include Professor R. W. B. Ellis, professor of child life and health in the University of Edinburgh; Professor K. V. Krishnan, professor of microbiology in the All-India Institute of Hygiene and Public Health; and Professor I. M. Thompson, professor of anatomy in the University of Manitoba.

Rations for Coeliac Disease.—The Ministry of Food announces that in future children with coeliac disease on a wheat- or gluten-free diet may be allowed one extra ration of fats, one extra meat ration, and one priority allocation of eggs a week as an *alternative* to the extra rations at present granted to such cases. It is also stated that the Ministry's medical advisers are prepared to give consideration to the cases of adults with steatorrhoea who are on similar diets. (P.N.6209a, September 8, 1952.)

Blood Donors Wanted.—The Ministry of Health is appealing for 145,000 more blood donors. Although during the June quarter blood donations reached the record post-war level of 161,880, and the number of donors on panels in England and Wales was also a record at 481,422, more blood is being demanded by the hospitals. If this trend continues either individual donors will have to be used more frequently or more donors must enrol.

Science and Industry.—A special section of the British Association is to be set up to study the application of science to industry. This was announced by Professor A. V. Hill at the final session of the Association's annual meeting in Belfast.

Upbringing of Young People.—A survey of the influences affecting young people is to be undertaken by King George's Jubilee Trust. Young people will be studied from the time they enter their primary schools until after their National Service. The main object of the investigation is to present a clear picture of the present position. The Trust, which was founded in 1935 to commemorate the silver jubilee of King George V, is the leading organization in Britain concerned with the welfare of the younger generation.

Dr. J. C. Gilson has been appointed director of the Medical Research Council's pneumoconiosis research unit in South Wales. He succeeds Dr. Charles Fletcher.

NEW ISSUES

Annals of the Rheumatic Diseases.—The next issue of this journal (Vol. 11, No. 3) will be available in a week's time. The principal contents include:

STENOSING TENOSYNOVITIS. G. Palmborg.
REHABILITATION AND TREATMENT BY MOVEMENT OF CONTRACTURES IN RHEUMATOID ARTHRITIS. Gunnar Edström.
EFFECT OF PLACENTAL "SERUM" IN RHEUMATOID ARTHRITIS. Jerome Simson and Joseph J. Bunim.
GOLD THERAPY AND NEUTRAL 17-KETOSTEROID EXCRETION IN RHEUMATOID ARTHRITIS. James Bruce and Robert MacKay.
GOLD-TESTING IN GOLD TREATMENT OF CHRONIC POLYARTHRITIS: RESULTS OF CONTINUED EXPERIMENTS. Tore Svanberg.
CLINICAL "ASSAY" OF CORTICOTROPHIN: PRELIMINARY COMPARISON OF METHODS. B. M. Ansell and E. G. L. Bywaters.
ULNAR DEVIATION OF THE FINGERS. Brandon Lush.
TUBERCULOUS RHEUMATISM: REPORT OF A CASE. P. G. Dalgleish.
COMPARATIVE EFFECTS OF CORTISONE, ACTH, AND DOCA IN A CASE OF RHEUMATOID ARTHRITIS WITH ADDISON'S DISEASE. Philip Ellman and Leon Cudkowicz.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d.

British Journal of Venereal Diseases.—The next issue of this journal (Vol. 28, No. 3) will be available in a week's time. The principal contents include:

POSSIBLE APPLICATIONS OF ADRENOCORTICOTROPHIC HORMONE (ACTH) AND CORTISONE IN SYPHILIS. G. O. Horne.
GONOCOCCAL INFECTION OF THE PARA-URETHRAL GLANDS IN THE FEMALE. Elisabeth Rees.
NEWER METHODS IN THE DIAGNOSIS AND TREATMENT OF GRANULOMA INGUINALE. Robert B. Greenblatt and W. E. Barfield.
STANDARDIZATION OF THE WASSERMANN TEST USING PRESERVED COMPLEMENT TITRATED TO 50% HAEMOLYSIS. P. N. Coleman.
SYPHILIS IN MENTAL DEFICIENCY. W. V. Macfarlane and C. B. S. Schofield.
AUREOMYCIN IN THE LOCAL TREATMENT OF TRICHOMONAS VAGINITIS. C. S. Nicol, E. Gallagher, and A. J. King.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d.

These journals are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

COMING EVENTS

Medical Protection Society.—The annual general meeting of the Society will be held at Victory House, Leicester Square, W.C.2, on October 1 at 3 p.m.

Clinical Pathology.—The 49th general meeting of the Association of Clinical Pathologists will be held on October 2, 3, and 4 at Westminster Hospital Medical School, London, S.W.1. Professor R. J. V. Pulvertaft will give the presidential address on October 3 on the individual and the group in modern medicine. As well as papers covering a wide range of subjects such as the testing of plasma and its fractions for anti-haemophilic potency (W. R. Pitney and J. V. Dacie), the tubeless test meal (J. Harkness and J. A. Durant), the Army T.A.B. vaccine (Lieutenant-General F. Harris), and the sensitivity and resistance of *M. tuberculosis* to isoniazid (R. Knox), there will be demonstrations and films. Full details of the programme of scientific sessions may be had from the honorary secretary, Dr. W. H. McMenemey, Maida Vale Hospital for Nervous Diseases, London, W.9.

Guy's Hospital Medical School.—The biennial dinner for past medical and dental students will be held in the Grand Hall of the Connaught Rooms, Great Queen Street, London, W.C.1, on Friday, October 3, at 7 p.m. for 7.30 p.m. Tickets 25s. each (inclusive of tips, but exclusive of wines) obtainable from Mr. O. Gayer Morgan, honorary secretary, Guy's Hospital Biennial Dinner, Medical School, Guy's Hospital, London, S.E.1 (telephone number HOP 3500, extension 383).

Royal Free Hospital.—Sir Henry Dale will give the inaugural address of the 1952–3 session on October 3 at 3 p.m. in the Beveridge Hall, Senate House, University of London.

St. George's Hospital.—Professor Sir David Hughes Parry will give the inaugural address of the 1952–3 session on October 4 at 3 p.m. at the hospital. The medical school dinner will be held the same evening at the Washington Hotel, Curzon Street, W.1.

Westminster Hospital.—Sir Raymond Evershed, P.C., Master of the Rolls, will give the inaugural address of the 1952–3 session on October 6 at 3.45 p.m. at Church House, Great Smith Street, S.W.1.

St. Thomas's Hospital.—The old students' dinner will be held at the Trocadero Restaurant, Piccadilly, W.1, on Friday, October 17, at 7 p.m. for 7.30 p.m. Tickets (£1 9s. exclusive of drinks) may be obtained from the honorary secretaries at the hospital.

University College Hospital.—Sir Wilson Jameson will give the opening address of the 1952–3 session on October 7 at 2.50 p.m. at the hospital. The annual dinner will be held on October 31 at 7.30 p.m. for 8 p.m. at the Savoy Hotel, Strand, W.C.2.

Welsh National School of Medicine.—Professor J. Henry Dible will give the inaugural address of the 1952–3 session on "Chance, Design, and Discovery" at 4.45 p.m., on October 9 at the medical school. The annual dinner will be held the same day at 6.45 p.m. for 7 p.m.

Birmingham Medical School.—Professor G. W. Pickering will give an address on "Opportunity and the Universities" on October 6 at 3 p.m. at the Queen Elizabeth Hospital to mark the opening of the academic year. An informal conversazione will be held in the medical school from 8 p.m. to 10 p.m.

Sheffield Medical School.—Sir Edward Mellanby will deliver the opening sessional address on "The Advance of Medical Science" on October 9 at 5 p.m. in the Firth Hall of the University.

Problems of Nutritional Research.—The full programme of the International Union of Nutritional Sciences' symposium being held in Basle, October 1 to 4 (see *Journal*, June 21, p. 1364), is now available, and details may be had from Dr. L. J. Harris, Dunn Nutritional Laboratory, Milton Road, Cambridge.

Institute of Dermatology.—The winter lecture course will begin on October 1, and the syllabus again includes lectures on subjects allied to dermatology. Systematic lectures will be given on Tuesdays, lectures and demonstrations on pathology, medical mycology, and *x*-ray technique on Wednesdays, and clinical demonstrations on Fridays. All lectures will be held at 5.30 p.m. at the Institute, Lisle Street, London, W.C.2.

London School of Hygiene Association.—There will be a dinner for members of the association at Frascati's Restaurant, Oxford Street, London, W.1, on Friday, October 17, at 6.30 for 7 p.m. (dinner-jackets). Each member may bring one guest. Tickets (£1 each) from Miss K. M. Shaw, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Wednesday, September 24

MIDDLESEX COUNTY MEDICAL SOCIETY.—At West Middlesex Hospital, Isleworth, 4 p.m., A.G.M. "*Personality in Medicine*," Chairman's Address by Dr. Marjory W. Warren.

Friday, September 26

●ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—At Royal Society of Medicine (Barnes Theatre), 1, Wimpole Street, London, W., 2.45 p.m., "*Percivall Willughby's Observations in Midwifery*," William Meredith Fletcher Shaw Memorial Lecture by Professor Miles H. Phillips.

APPOINTMENTS

BRODIE, N. H., M.B., Ch.B., House-surgeon, Stanley Hospital, Liverpool.

CAREY, A. S., M.B., Ch.B., D.P.H., Deputy Medical Officer of Health, Burton-on-Trent.

DE FONSEKA, C. P., M.B., B.S., F.R.C.S., Surgical Registrar to Bath Group of Hospitals, South-western Regional Hospital Board.

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BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brandon.—On August 21, 1952, at the Women's Hospital, Derby, to Joan (formerly Hallows), wife of Dr. Richard Brandon, a daughter.

Duguid.—On August 31, 1952, at Liverpool Maternity Hospital, to Mary (formerly Barry), wife of John Duguid, M.B., Ch.B., a daughter.

Guest.—On August 22, 1952, at Nachingwea Hospital, Tanganyika, to Ilse, wife of Dr. J. G. Guest, a second son—Michael Ernest.

Illingworth.—On September 13, 1952, at the Jessop Hospital, Sheffield, to Cynthia (formerly Redhead), M.R.C.P., wife of Professor R. S. Illingworth, F.R.C.P., a daughter.

Kelly.—On August 31, 1952, at Mayday Hospital, Croydon, to Audrey (formerly Worman), M.B., B.S., D.C.H., wife of Eric M. Kelly, a daughter—Katharine Jane.

Mitchelmore.—On August 29, 1952, to Una (formerly Pearce Jones), M.B., Ch.B., wife of Gordon Mitchelmore, M.B., Ch.B., of The Croft, Wallingford, Berks, a son—Andrew Edward.

Moselhi.—On September 2, 1952, at Carlisle, to Margaret Mary, wife of Dr. A. Moselhi, a son.

Sudbury.—On September 5, 1952, at Wolverhampton, to Mary (formerly Sadler), wife of Dr. J. R. Sudbury, a daughter.

Wand.—On September 5, 1952, at Rush Green Hospital, Romford, Essex, to Betty (formerly Manders), wife of Dr. Laurence G. R. Wand, a son.

MARRIAGES

Grey Turner—Tomlinson.—On July 26, 1952, Elston, son of the late Professor G. Grey Turner and of Mrs. Grey Turner, to Lilias, daughter of the late Colonel S. C. Tomlinson and of Mrs. Tomlinson.

DEATHS

Andrews.—On September 2, 1952, at "Gorse," Blatchington, Seaford, Sussex, Henry Arthur Andrews, M.R.C.S., L.R.C.P., formerly of Tonbridge, aged 80.

Bailey.—On August 31, 1952, Thomas William Bailey, M.R.C.S., L.R.C.P., of 28, Flora Grove, St. Albans, Herts, formerly of Orpington, Kent, aged 84.

Barnes.—On August 30, 1952, John Arthur Percival Barnes, M.R.C.S., L.R.C.P., of 819, High Road, Tottenham, London, N., aged 76.

Barr.—On September 7, 1952, at Edgcumbe House, Eliot Gardens, Newquay, Cornwall, Oliver Flett Barr, M.B., Ch.B., aged 57.

Chisholm.—On September 6, 1952, John Douglas Chisholm, M.D., of "Kingsfield," Northenden Road, Sale, Cheshire.

Fosbrooke.—On August 31, 1952, at Browside, Gateacre, Liverpool, John Malcolm Fosbrooke, M.B., F.R.C.S.Ed., aged 46.

Hemmant.—On September 11, 1952, at Dockwray Cottage, Grasmere, Lynette Hemmant, M.R.C.S., L.R.C.P., aged 70.

Hutchison.—On September 13, 1952, at Point House, Magdalen Road, Norwich, Thomas Todd Hutchison, M.B., Ch.B.

Innes.—On August 24, 1952, at Grantown-on Spey, Inverness-shire, Flora Riddell Innes, M.B., Ch.B., formerly of the Christian Medical College, Vellore, Madras, India, and Brisbane, Australia.

Jefferiss.—On September 7, 1952, at Totnes, Devon, Ian Mackinnon Jefferiss, M.R.C.S., L.R.C.P.

Kittel.—On September 7, 1952, at his home, 12, Bridge Street, Hungerford, Berks, Paul Bruno Kittel, F.R.C.S., of 44, Queen Anne Street, London, W.

Letcher.—On September 10, 1952, at 51, Woodhurst Road, Acton, London, W., Herbert George Letcher, M.B., F.R.C.S.

Mackenzie.—On September 12, 1952, at Edinburgh Royal Infirmary, Rachel Elizabeth Woodman Mackenzie, M.B., D.P.H.

Menzies.—On September 2, at Davyhulme Hospital, Manchester, Duncan Menzies, L.M.S.S.A., D.M.R.E., of Hawthorn Cottage, Comberbach, Northwich, Cheshire, aged 61.

Ormrod.—On September 5, 1952, Peter Richard Ormrod, M.R.C.S., L.R.C.P., of 1, Cedar Road, Chasetown, Staffs, formerly of 41, Sneyd Avenue, Newcastle-under-Lyme, aged 30.

Parkinson.—On September 12, 1952, at 58, Thames Drive, Leigh-on-Sea, Essex, Kathleen Hazel Parkinson, M.R.C.S., L.R.C.P.

Pollard.—On September 3, 1952, at Pound Hill, Framfield, Sussex, Sidney Pochin Pollard, M.D.

Robinson.—On September 2, at Lingfield Lodge, East Grinstead, Sussex, William Edward Robinson, M.D., M.R.C.P., aged 82.

Rosenberg.—On August 27, 1952, Ernst Rosenberg, M.D., of 10, Westbury Road, Woodside Park, London, N.

Ross.—On September 9, 1952, at 8, Scott Road, Tarbert, Inverness-shire, Victor Alexander Ross, M.B., C.M., J.P.

Sankey.—On September 1, 1952, at 44A, Copers Cope Road, Beckenham, Kent, William Octavius Sankey, M.D.

Scott.—On September 7, 1952, at Abingdon, Berks, Charles Robert Scott, O.B.E., M.B., C.M.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Post-streptomycin Vertigo

Q.—*What treatment is recommended for post-streptomycin vertigo? A patient under my care was successfully treated with streptomycin for tuberculous salpingitis, but ever since has suffered from great unsteadiness with a tendency to fall to the left side and marked incoordination of the left arm and leg, together with constant ringing in the left ear but without impairment of hearing. Would surgical division of the eighth nerve help in this case?*

A.—Vertigo following streptomycin therapy indicates impairment of vestibular function. Usually both labyrinths are equally affected, but one may be more damaged than the other. It may be found in the patient in question that the left vestibular labyrinth is more severely affected than the right, but this can be assessed accurately only after a caloric test of vestibular function. At the same time it would be advisable to carry out a complete test of hearing, including a pure-tone audiometer test.

The lesion in these cases is usually irreversible. Surgical treatment, either by division of the eighth nerve or by labyrinthectomy is rarely necessary. Most cases respond well to the head and balancing exercises which are used for the treatment of giddiness due to vestibular damage following head injuries or operation on the labyrinth. These were described fully by Cawthorne and Cooksey (*Proc. roy. Soc. Med.*, 1946, **39**, 270), and their paper should be consulted for further details.

Detection of Anaemia

Q.—*How reliable is inspection of the conjunctivae in the detection of moderate anaemia? Is there any better clinical test?*

A.—Pallor of the mucous membranes is certainly a more reliable sign of anaemia than pallor of the skin, though even so it is not a sensitive test. Attention should not be confined to the conjunctivae, as they may be deceptively red if they are inflamed, and the lips in women are nowadays rarely left in their natural state. The appearance of the mucous membrane of the mouth, particularly of the soft palate, is often a better guide. There is no other direct clinical test for anaemia, but indirect evidence is sometimes provided by collateral evidence of a deficiency of iron or the liver factor, which may be revealed by spoon nails, glossitis, or angular stomatitis.

Throat Pack for Facio-maxillary Surgery

Q.—*Could you please recommend a throat pack for facio-maxillary surgery which will not cause a sore throat? At present I use an endotracheal tube lubricated with liquid paraffin and then pack with wide ribbon-gauze autoclaved after soaking in paraffin. The pack must catch debris as well as soaking up blood.*

A.—The wording of this question suggests that the character of the throat pack is the sole factor in causing the sore throat. This is not so. The way in which the pack is inserted is also of great importance. No improvement in the nature of the pack or the way in which it is sterilized can be suggested, but the pack must be inserted with the greatest gentleness. The anaesthetist should stand facing the patient and, using a tongue depressor, insert the pack gently with his fingers, gloved for preference so that his finger-nail does not traumatize the palate or pharynx. On removal of the pack a tongue depressor should again be used and the ribbon-gauze withdrawn slowly and with the greatest care. Rough insertion and removal of the pack, and trauma to the palate and fauces by instruments and finger-nails, are common causes of sore throat; they are probably as important in its causation as the nature of the pack itself.

Cortisone and A.C.T.H. for Exfoliative Dermatitis

Q.—*One of my patients, a girl of 14 years, has been suffering from primary exfoliative dermatitis for the last six months. There has been no improvement in her condition in spite of the thorough empirical treatment advised in standard textbooks on dermatology. Is cortisone or A.C.T.H. of any value in this disease?*

A.—Excellent results have indeed been obtained in the treatment of exfoliative dermatitis with cortisone and A.C.T.H. In the writer's experience the dose of A.C.T.H. likely to be required in an adult is in the region of 25 to 30 mg. four times daily. In this case it is suggested that the commencing dose should be 10 or 15 mg. four times daily, and that this be slowly increased until response is obtained. In a favourable case the cessation of itching and the return of the skin to normal take place within a few days. The dose should then be progressively reduced until a satisfactory maintenance dose can be determined. In most cases a maintenance dose will be needed, perhaps for a few months, but it is likely that the hormone can be withdrawn altogether eventually and the patient remain well. Similar good results have been reported, principally in the United States, from the use of cortisone. The dose required is likely to be considerably smaller, probably in the region of 15 to 25 mg. daily.

Are More Babies Born at Night?

Q.—*Is there anything in the impression that a disproportionate number of births occur during the night? If so, does this represent a biological survival?*

A.—The impression that more babies are born during the night than during the day is a false one. It probably arises because most labours last longer than 12 hours and the phase which encroaches on the night hours is more often remembered. Several statistical inquiries on this point have been conducted during the last 40 years, and these go to show that there is little, if any, significant difference in the number of births taking place between 6 a.m. and 6 p.m. and between 6 p.m. and 6 a.m. The difference in favour of night time is not more than 2 to 5%. One analysis suggested that there may be slightly more babies born between 9 p.m. and midnight than in the other three-hourly periods.

Plasma Substitutes in the Tropics

Q.—*In the Tropics human plasma is rarely available for transfusion, and it is also often exceedingly difficult to overcome a natural aversion to blood transfusion on the part of both donor and recipient. Is it likely that gum arabic would prove a useful substitute, and, if so, how is it prepared for transfusion? Can you recommend any alternatives?*

A.—Gum saline solution (gum arabic), although still used and available commercially, has fallen generally into disfavour because of various reports that gum may be stored in the liver, spleen, bone marrow, etc., is only slowly excreted, and may be associated with severe reactions, sometimes fatal (see references below). Apart from the possibility that these effects may be produced, gum saline will satisfactorily restore a depleted blood volume. The local preparation of gum saline in solution is not recommended. Of the more recent plasma substitutes dextran has been widely used in Scandinavia and, to a lesser extent, in Great Britain, and polyvinylpyrrolidine has been used in Germany

and France, and also in Great Britain. Both are made commercially in Great Britain and appear to be safe and effective if used with discretion, but their relative merits cannot yet be assessed. Gum saline costs approximately 6s. per bottle (500 ml.); dextran and polyvinylpyrrolidine cost about 35s. and 30s. per bottle (500 ml.) respectively. Retail prices are quoted.

Plasma substitutes find their main use as agents for the temporary restoration of blood volume; they should not be given in quantities which will dilute the haemoglobin and plasma protein to dangerously low levels. The infusion of plasma substitutes cannot, of course, replace the transfusion of blood, for which there is no substitute.

REFERENCES

Andersch, M., and Gilson, R. B. (1935). *J. Pharmacol.*, **52**, 390.
Dick, M. W., Warweg, E., and Andersch, M. (1935). *J. Amer. med. Ass.*, **105**, 654.
Mannix, E. P. (1947). *Brooklyn Hosp. J.*, **5**, 200.
Studdiford, W. E. (1937). *Surg. Gynec. Obstet.*, **64**, 772.

Prolonged Use of Ephedrine

Q.—*Are there any dangers in the prolonged use of ephedrine hydrochloride tablets for asthma? A patient now receives 90 gr. (6 g.) a week. Less makes him unhappy. What are the symptoms of addiction and how can they be treated?*

A.—There are no dangers in the prolonged use of ephedrine. Chronic intoxication from its repeated administration is unknown. With regular use, especially when taken three times a day or oftener, the body soon develops a tolerance for ephedrine which renders it less and less effective even with increasing dosage. When this tolerance develops the drug should be stopped for four or five days or so, after which the primary dose will again be found to be effective.

Addiction to ephedrine does not occur, although it is not infrequent for patients to be nervous of leaving it off because of their fear of more severe attacks developing, while a few like its slightly stimulating effect. The importance of leaving it off for a few days should be explained to the patient and other preparations, such as *iso*propyl-*nor*-adrenaline, aminophyllin, neb. adrenal. et atrop. co. (*N.F.*), or a preparation of caffeine, such as elix. caffein. iod. (*N.F.*), can be tried instead. It might be advisable to find which preparation gives relief before stopping the ephedrine completely.

Intractable Pruritus Vulvae

Q.—*What are the likely causes of a severe pruritus vulvae, now extending to the perineum, perianal region, and buttocks, which has twice remitted completely during pregnancy and lactation? On the first occasion the remission had started before the patient realized that she was pregnant. There is an associated seborrhoeic dermatitis of the head and trunk. Treatment in expert hands by hormones, local applications of all kinds, and x rays (two courses) has been unavailing. The patient is 38 and psychologically stable. What treatment is advised?*

A.—Your questioner omits to mention whether the vulva and perineum are objectively normal in appearance. As there is an associated seborrhoeic dermatitis of the head and trunk a similar involvement of the perineum must, of course, be excluded. In this situation seborrhoeic dermatitis is common and is often complicated by secondary infection, giving rise to a form of intertrigo. Lichen sclerosus et atrophicans is another common cause of pruritus in this situation and may be complicated by leukoplakia. Gynaecological causes and urinary abnormalities have presumably been excluded.

The idiopathic form of pruritus in which the skin shows no change other than that produced by friction is the most difficult to treat. Since many other methods have been used in this case without avail, subcutaneous infiltration with benzocaine or alcohol, such as is practised for pruritus ani, might be seriously considered.

The Electrified State

Q.—*I have an elderly lady patient suffering from Parkinson's disease who appears to be charged with static electricity. On stroking her skin a definite tingling sensation is experienced in varying and inconstant places which is similar to the feel of a very high frequency tuning-fork. This sensation is more noticeable if the examiner uses the dorsum of his hand, is not related to the degree of tremor, and seems most marked over parts that at that moment are painful. It has been noticed by several observers—her husband, nurses, a physiotherapist, and myself. Can it be explained, and is it of any clinical significance?*

A.—The sensations are very likely due to an electrified condition of the patient—some people easily accumulate charges of static electricity. They behave, on a large scale, like the vulcanite fountain-pen which, when rubbed on a sleeve, will pick up shreds of paper. This property is probably dependent upon physical factors, such as the dryness of the skin. The "electrified state" is probably of little clinical significance. In suitable circumstances such people may feel and even see and hear the discharge spark which occurs when they touch earthed metallic objects.

Intravenous Morphine

Q.—*When giving morphine intravenously—for example, in road accidents—can the contents of the usual ampoule be given undiluted? Is the dosage the same as by other routes?*

A.—The answer to the first part of the question is in the affirmative. The usual dose of ½ or ¼ gr. (11 or 16 mg.) can be given intravenously, but it is unwise to give by this route the larger doses of morphine sometimes given subcutaneously or intramuscularly, such as ¼ or ½ gr. (22 or 32 mg.).

Persistent Hiccup

Q.—*Where can I find information on the treatment of persistent hiccup?*

A.—On p. 112 of the book *"Any Questions?"* The book can be obtained for 7s. 6d. (postage 6d.) from the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

NOTES AND COMMENTS

Motion-sick Infants.—Dr. E. J. R. PRIMROSE (Brora, Sutherland) writes: Your consultant answering the question about motion-sick infants ("Any Questions?" September 6, p. 574) may be interested to know that my eldest daughter was seasick when 4 months old during a crossing of the Pentland Firth during one of its viler moods. She continued to have motion sickness till she was about 4 years old.

Dr. A. C. LEVINSON (London, N.10) writes: My daughter showed definite symptoms of this condition on a short sea journey of 45 minutes, when she was 8 months of age. She was sitting in the pram, became very pallid, and lay down. She had completely recovered within three minutes of landing on the pier.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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